Transactions of the Medico-Chirurgical Society of Edinburgh

SESSION CI.—1921-1922

At a Meeting held on 5th November, the following gentlemen were elected Office-bearers for the Session 1921-1922:—

President

Sir ROBERT PHILIP.

Vice-Presidents

Dr JOHN THOMSON. | Dr WILLIAM STEWART.
Sir DAVID WALLACE.

Councillors

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Mr J. W. DOWDEN. | Mr D. M. GREIG.
Emeritus Professor F. M. CAIRD. | Mr GEORGE CHIENE.

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Dr MACRAE TAYLOR,
8 Melville Street.

Secretaries

Dr WILLIAM T. RITCHIE,
14 Rothesay Place.

Mr W. J. STUART,
9 Chester Street.

Editor of Transactions

Dr CHALMERS WATSON,
11 Walker Street.

Transactions of the Medico-Chirurgical Society of Edinburgh

VALEDICTORY ADDRESS*

By The PRESIDENT, Mr F. M. CAIRD.

THERE still remain certain duties to perform before relinquishing the high position with which you honoured me two years ago. First comes the grateful task of returning my heartfelt thanks to this venerable—I may now say venerable—Society for the distinction they conferred upon me, and may I also express my keen appreciation for the uniform sympathy they have on all occasions accorded to the halting efforts of their President. You will expect to receive a reference to the events of the past Session, and I shall thereafter give a short survey, a retrospect of the history of our Medico-Chirurgical of Edinburgh since its institution in 1821.

Permit me to exercise brevity in paying reverential tribute to the memory of our Fellows who have passed away during my term of office. Appreciative obituary notices of each appeared in the leading Medical Journals at the dates of demise undermentioned.

Our distinguished Fellow, Sir William Osler (æt. 70, ob. December 1919), occupied a unique position in the medical world. His engaging mentality, the style and grace of his literary achievements and his catholicity made him leader, guide, philosopher, and friend. We estimate highly the worth of the eminent scholar from Canada, who so fitly adorned the Chair of Medicine in the ancient University of Oxford.

Two names have fallen from our list of Corresponding Members. Raphaël Lépine (æt. 79, ob. November 1919), Professor of Clinical Medicine at Lyons, was a great clinician, renowned for his researches in Therapeutics and his work on Diabetes, on Cerebral Localisation, and Neurology.

* Delivered 2nd November 1921.

David Lloyd Roberts (æt. 85, ob. Oct. 1920), the well-known gynæcologist and pioneer in Obstetric Surgery of Manchester, possessed versatile attainments. An art collector and successful practitioner, he bequeathed of his large fortune generous gifts to medical ends and charities.

Our Society has also suffered sad loss in the ranks of the Ordinary Fellows.

Sir Thomas R. Fraser (æt. 78, ob. Jan. 1920), the accomplished physician and eminent Professor of Materia Medica, has left his imprint on generations of pupils and teachers. Our Meetings were for many years enlivened by the presence of the alert, thin figure, vibrant with nervous energy, couching his phrases in choice fluent English as in Communications and debate with swift rapier-like flashes, he contended for scientific accuracy and precision. At present it must suffice to record our admiration for the indomitable investigator and lucid lecturer, so long a loyal supporter of our Meetings.

David Berry Hart (æt. 68, ob. June 1920), of most original and fertile mind, gifted with a retentive memory stored with cyclopædic learning, was a doughty champion in the ranks of progress and research. Filled with enthusiasm for his profession and his school, Hart's anatomical, developmental, and gynæcological work remains classic. A staunch friend, single-hearted, energetic, and industrious, he continued his manifold literary activities unabated till the end.

Arthur Neve (æt. 62, ob. 1920) gave his life to missionary enterprise amidst the hills of far Kashmir. There his labours and surgical skill overcame the barriers of race and religion with such acceptance that he was accorded a public funeral by the Maharajah. He rendered valuable service during the Great War, and while carrying out his missionary expeditions found time to extend our knowledge of Himalayan geography.

David Yellowlees (æt. 85, ob. Jan. 1921), the veteran alienist, long associated with the Gartnavel Asylum.

We have also to chronicle the deaths of John MacRae (ob. Feb. 1919); Skene Keith (ob. Aug. 1919), son of the ovariotomist, Thomas Keith; Hugh L. Calder (ob. Nov. 1919) of Leith; J. Batty Tuke (æt. 60, ob. June 1920), son of the late Sir John Batty Tuke; the cultured George Thyne (æt. 52, ob. June 1920); the lovable J. W. Simpson (æt. 48, ob. Jan. 1921); the Hon. Donald Macaulay (ob. March 1920) of the Cape Legislature, a perfervid and loyal Scot, killed by motor

accident; and lastly, that of the courteous George Hunter (æt. 79, ob. Oct. 1921).

We mourn the severance of friendships. Death has called many of our Fellows. May they rest in peace.

The General Meetings of our Society, held latterly for some time in the Victoria Dispensary, thanks to the kindness of Sir Robert Philip and his Committee, have taken place since June 1920 in the New Gallery, Shandwick Place, which seems to be, on the whole, a more convenient centre.

Twenty-four papers were read, covering a wide range of subjects. They were all of high standard, and several of such outstanding excellence that the Society may well congratulate itself.

It is an interesting point that the majority of Communications dealing with war studies were furnished by physicians.

The special Discussions attracted a large attendance, and the Society was favoured by the presence of many visitors, who either inaugurated or participated in the debates.

These Discussions were six in number. They were devoted to a consideration of: Psychotherapy, opened by Prof. G. A. Robertson; The Treatment of Tuberculosis, introduced by Sir Robert Philip, and followed by Sir Henry J. Gauvain on Non-pulmonary Tuberculosis; Enteroptosis, by Dr Chalmers Watson, after a lantern demonstration by Dr Hope Fowler. Professor Arthur Robinson also took part in this Discussion. Physical Therapeutics, opened by Dr Stuart Ross; Treatment by X-rays and Radium, by Dr Knox, London; Physical Education in the Universities of the U.S.A., an Address by Prof. Tait M'Kenzie, University of Pennsylvania.

The four Clinical Meetings in the Royal Infirmary provided a wealth of material, illustrating, amongst others, types of various cardiac affections, diseases of the blood, anæmias, disorders of the digestive and nervous systems. Striking examples of successful operative procedures on the alimentary and renal tracts, on the larynx and œsophagus, on the brain, on the head, on the nose, on the extremities, were also presented.

Worthy of record is Dr Gertrude Herzfeld's Enterectomy for gangrenous ileum in a baby only twelve days old. The infant had suffered from strangulated hernia, and made a perfect recovery.

The activity of the past Sessions leads us to anticipate a continuation of good work, and gives reason to hope that general practitioners and those who hold hospital charges may vie with each other during the coming Session in promoting the high ideals and weal of our Society. Our membership roll at present stands at high-water mark.

Gentlemen, it is now one hundred years since Dr Robert Hamilton, teacher of Ophthalmology in this city, circulated amongst the profession a paper in which was written, "By subscribing our names to this paper we testify our approval of the objects and constitution of the Medico-Chirurgical Society of London, and our willingness to co-operate in the formation of a similar Society in Edinburgh." Fifty-three names were speedily appended, and on 2nd August 1821 our Society was instituted. The first President was the time-honoured Dr Andrew Duncan, Senior, well known to us all as founder of the Royal Public Dispensary and of the Royal Asylum. The Secretaries were Dr Robert Hamilton, Mr Russell and Dr Alison.

The Society prospered, especially fostered by the College of Physicians, who generously granted it a room in which to meet. The place of meeting has, however, varied, for the Society has not been able to attain the object so long desired, namely, a hall of its own. During the first fifty years of its existence, from 1821 to 1871, our Members witnessed and discussed the current phases of medical thought and treatment. They participated in the rise and wane of blood-letting as a general panacea, and the very names "Cupper" and "Clogger" are now obsolete—extinct as the Dodo. They took part in the common pouring of the proverbial little-known drug into the still less known human frame, and they exhibited purges and draughts enough to rejoice the exponents of ileal stasis, as they cleared out a toxic flora from the intestinal tube. They witnessed pre-antiseptic surgery at its best under the master-mind and cunning hand of Syme, and may have read with satisfaction the dictum that surgery could no further go, so near was it to perfection. And yet the lament of Pirogoff might be heard groaning over the awful game of chance which the surgeon had to share, a veritable *rouge et noir*, wherein the odds were great. They also were blessed as they realised and eagerly grasped the transformation wrought by anæsthesia, and there was never a more

epoch-making night in our annals than in November 1847 when Simpson produced his historic paper amidst the applause and wonder of a crowded audience. Nor has the experimental dissipation with the new drug, which concluded the after-proceedings, ever been equalled. They heard also, and doubtless largely shared in, the condemnation of those intrepid surgeons who had made outrageous attempts to invade the sacred precincts of the abdominal cavity, but later had to yield to the powerful advocacy of Simpson in favour of ovariotomy, and still later to witness and welcome the triumphs of Thomas Keith. The wondrous protective powers of the peritoneum, under due guidance, are now manifest to all of us.

Towards the close of our first fifty years, the morning of new light was breaking, heralded by the golden dawn ushered in by Faraday, Darwin, and Pasteur. Already the mighty orb of Lister appeared above the horizon. The man and the hour had come.

Abundant reference to what was taking place and what had been already accomplished, may be found in the "Jubilee Chronicon" published in the *Edinburgh Medical Journal*, 1874. This was the Valedictory Address of Dr P. H. Handyside. Handyside, after a somewhat interrupted career, became lecturer in Anatomy in the Surgeons' Hall, was our President in the year 1871, when he entertained the public to a Jubilee Conversazione in the Freemasons' Hall. At that time three veterans, original Members of the Society in 1821, were yet alive, and this appears a fitting place to note that, of the many Fellows of our Society who took part in that Jubilee, there are still a few happily well, among whom we may mention Professor John Chiene, C.B., who was then one of our Secretaries, and who showed a modified hot stage for the microscope at the Conversazione, as also Dr M'Kendrick, afterwards Professor of Physiology in Glasgow, now of Stonehaven, and the veteran Dr William Craig, Editor of the *Transactions*, now in his 90th year.

The past fifty years, from 1871 to 1921, has displayed most marvellous advance in our profession, as science progresses rapidly onwards, gaining in velocity and mass. We have alas, also received the sad lesson that the greatest intellect, inventive genius and science which seemed destined to further the cause of humanity, can be perverted and squandered to evil ends and destruction.

The new period, so full of promise and hope, saw the antiseptic system accepted. Cradled in Glasgow, it grew to lusty, world-compelling youth in Edinburgh. It obliterated the reproach of Pirogoff; doubts, sepsis, and disaster were replaced with sweet certainties. The germ theory firmly established, the study of micro-organisms and bacteriology grew apace. Physiology and pathology gave us new and correct conceptions, and thus treatment founded on a scientific basis, no longer purely curative but hopefully phylactic, stretches far beyond the bedside of the poor hospital patient into the highway of hygiene and public health. So extensive now is the domain of our art, that specialisation has become a necessity, and threatens to swamp or cramp education on broad general principles. A limitless future lies before us. Into the various and marvellous departures, fresh to us every day, we shall not now venture.

The old records of our Society, its Minute and Council Books, are filled with historic matter, at least of local interest. We may therein peruse the handwriting and signatures of many well-known names and illustrious men who well served their day and generation, and with lasting result. True it is that we meet evidence of stormy times when blood ran hot, perhaps giving support to the old theory that fevers have changed their type from sthenic to asthenic, so that blood-letting becomes no longer requisite. We need not regret that in our day a more charitable feeling obtains, nor have we entirely lost love of fair play.

The Proceedings of our Society have been continuously published, with the exception of the silent interval during the late war, when our energies were otherwise directed, and so many of our profession perished for King and Country. At first the publication took the form of *Transactions*, and three volumes were issued in 1824, 1825, and 1829. Following on this, our Reports appeared in the *Monthly Journal of the Medical Sciences* till 1855. Thereafter the *Edinburgh Medical Journal* carried on accounts of our Meetings till 1880. Then we once more resumed publication of separate *Transactions*, up to the present date. As you are aware, we have now under consideration the most available form in which to publish our Reports, suitable to our exchequer and the expense of production. A valuable index to the first twenty volumes of the new series of *Transactions*, from 1881 to 1901, was compiled

by our enthusiastic Editor, Dr William Craig. He also contributed a paper on the early publications of our Medico-Chirurgical Society in Vol. III., 1883-84.

I am tempted to recur to the main object of our Society. It is an educative striving after truth. Truth is notoriously elusive, often difficult to grasp, but with time aiding, becomes supremely definite. Fortunately its quest in cultured lands renders it open to all, giving freedom of intercourse. By this intercommunion, and by historic research, we are brought in contact with much which can be further tested at the touch-stone of experience. We are, however, apt to forget that judgment is difficult; experience fallacious. Our profession abounds in credulous minds, prone to go astray. Unfortunately, also, they minister to a still more credulous public, thus leading to instability of trust and hope. There is some excuse for an optimistic credulity begotten of the humane longing to seize every straw that may alleviate pains or assist in prolonging life. But there is greater reason to walk warily and to cultivate a sane scepticism, rather than accept theories and propositions before their worth has been proved. We know how our worthy forefathers were occasionally mislead by flights of imagination, and not only unwittingly hypnotised their patients into belief of some particular treatment, but they also hypnotised themselves —and that successfully. Have we not all had similar experiences? Can we not recall *ex cathedra* statements taken as gospel by ingenuous students. Some of us in bygone happy student days listened to the fascinating romance of *Bathybius Hæckelii*, that sheet of primordial protoplasm lining Atlantic depths, and was it not also provided with possible sense organs —coccoliths and coccospheres? Was it not suggested that this represented the beginning of all life, and what more natural than that it should be recognised, in a fossil state—the *Eozoon canadense!* Have we not been in our lifetime offended by the malodorous fumes of sulphuretted hydrogen injected into the bowels of trusting patients as treatment for tuberculosis? Have we forgotten the huge Gaiffe batteries that awoke our curiosity when the Apostoli treatment was all the vogue as the only sure and safe cure for uterine myomata? Has all this passed like Hans Breitmann's Barty—"Away in die ewigkeit"? Is it not fresh in our memory, that during the war an astounding method of mapping-out hæmorrhagic lesions of the brain and viscera by some so-called X-ray method was figured and pro-

mulgated? The scheming discoverer went a step too far, for from amongst the disciples of Hippocrates—to whom all human life is sacred—he sought transference to the ranks of Mars, having devised a secret method of destroying life by electrical forces manipulated at a distance—and shortly he and his schemes were seen no more. What do we hear now of the dielectric oil and the mysterious electric rod, which evidently captured the support of educated men about the same time, and were vaunted as new therapeutic agents. One may recall a remark of the sage Dr Matthews Duncan addressing his class, "Gentlemen, there are more quacks in the profession than out of it."

How marked is the contrast to what has been cited, in the abiding character of the principles formulated by Lister in regard to wound treatment. They stand now unchanged as they were written in 1867. Let us recall the logical simplicity of Koch's postulates. Let us remember that Ricord prophetically called syphilis the "Key" to all pathology, and note the sequence after Schaudinn's detection of the spirochæte, the rapid advances in methods of diagnosis, and the ideal treatment by Ehrlich's great sterilisation through the blood-stream. I well remember Neisser saying: "Salvarsan is altogether wondrous, beautiful—that it is a perfect cure, ask me twenty years hence!" The wise practitioner preserves a level mental equilibrium, knowing that we must possess our souls in patience and in hope. We may well marvel at the clinical insight of our forefathers, and recognising all the advantages we enjoy, be prepared for increasing change, as clinical research and pathology lifting the veil may enable us by prophylaxis and cure to solve the many problems that are waiting. We do not fear that our profession will ever drift into therapeutic Nihilism. Whatever changes may yet ensue, there will always remain the sympathetic bond of common humanity between practitioner and patient, the healing power of mutual trust and confidence.

One word more; our profession has received general recognition from a grateful public as an unselfish brotherhood. It must again feel that in these hard times, when loaves and fishes are but scant, that it has received unwonted homage and honour, and indeed the highest of honours, when those of its body more or less thirled to State control, have been selected to make a voluntary vicarious sacrifice to their love of country. Possibly, "needs must when the De'il drives." But notwithstanding, this

action on the part of a patriotic Government may be regarded as a great compliment.

Let me now say how much I owe to the Office-bearers and Members of Council who have so willingly and efficiently lightened the duties associated with the Chair. To Mr George Chiene, our Senior Secretary, who to-night vacates his onerous post, a meed of praise is due. My last and most agreeable function is to congratulate the Society in the able guidance it will enjoy under the rule of my distinguished successor, Sir Robert Philip, who accepts the new honour to which you have promoted him as President of the Edinburgh Medico-Chirurgical Society.

In moving a vote of thanks to the retiring President, Mr C. W. Cathcart recalled the early days in Mr Caird's career, when by his energy and skill he had assisted the late Dr Berry Hart to good purpose in making frozen sections of the female pelvis. These qualities, combined with a broad outlook, wide reading, and unfailing courtesy, had enabled Mr Caird to help many others since that day, and had been applied with much success to the business of the Medico-Chirurgical Society during the last two years.

Mr Cathcart had much pleasure in moving a hearty vote of thanks to Mr Caird for his valued services as President, and for his interesting Valedictory Address.

SIMPLE ENLARGEMENT OF THE PROSTATE.*

By Sir DAVID WALLACE.

It is fitting, I think, that I should preface my remarks by referring to the late Sir Peter Freyer. May I say that in my view, although he claimed in some respects regarding the operation of prostatectomy more than he was entitled to, it was in virtue of his work that the operation was accepted by the profession generally, and that it was to him that this satisfactory method of treating this common and extremely disabling affection was made a practical proposition.

Simple enlargement of the prostate is a comparatively common affection in men over fifty years of age. Its etiology has not yet been satisfactorily determined. No theory which has been hitherto advanced suffices to explain why it should occur in some men and not in others. I do not propose to discuss the etiology and pathology, I wish rather to consider the subject from its clinical aspect, and in particular I desire to raise the question of treatment in early cases in which the symptoms are of recent origin. In the first place, however, we must recognise that symptoms which are frequently due to simple enlargement of the prostate may be caused by conditions in which the prostate is not enlarged or in which enlargement is caused by the presence of a malignant tumour. The recognition of these causes is of the greatest importance, but unfortunately it is not always easy to diagnose them. There are three in particular to which I shall shortly refer, viz. (1) stenosis at the neck of the bladder; (2) the small fibrous prostate, and (3) malignant disease.

Stenosis or contracture at the neck of the bladder gives rise to over-distention of the bladder, which comes on very slowly, and not infrequently when the patient consults his medical man the bladder is high in the abdomen, the only symptom being frequency of micturition associated with a great increase in the quantity of urine, which is of low specific gravity. Cystoscopy in such cases is frequently most helpful. A small fibrous prostate causes very similar symptoms, while a carcinoma of the prostate as a rule gives rise to symptoms similar to those caused by a simple enlargement, but the diagnosis is frequently comparatively easy from the hardness

* Read 2nd November 1921.

and nodular condition of the prostate, together with the fixation of the prostate as a whole.

Any one of these conditions may produce symptoms which closely resemble those due to simple enlargement, and if an error in diagnosis be made—and sometimes to differentiate is very difficult—an operation may be recommended and the prognosis stated to the patient and relatives be unduly optimistic—operation is carried out and found to be unsatisfactory. If there be a doubt in the mind of the surgeon, cystoscopy, which may help, should be adopted. Now grant that a patient suffers from a simple enlargement of the prostate which is causing symptoms, namely, some frequency of micturition—the patient requires to rise in the early morning—there is slight delay in the commencement of the act, and the stream is not so forcible as formerly. Perhaps if he drinks tea in the afternoon it produces an insistent desire to micturate, or it may be that he finds he must micturate every three or four hours during the day. In any case, the symptoms are an inconvenience to him. On examination per rectum the prostate is enlarged, smooth, elastic, and mobile—what advice should be given?

I naturally recognise that residual urine is a determining factor in the production of prostatic symptoms, but I do not advocate the passage of a catheter to enable the amount present to be estimated in a given case. When small in amount it does not in my opinion add to the justification of operation, and I think that the disadvantage of catheterisation is greater than any advantage to be gained by it. Further, in a case where the question of operation is hanging in the balance, the passage of a catheter may do harm and induce symptoms which may necessitate operation—I refer to retention following catheterisation, or cystitis due to sepsis. I deprecate the use of the catheter except incident to treatment.

Should prostatectomy be advised? Before answering this question let me say that no fixed rule can be laid down, each case must be considered by itself on its merits. Can improvement be expected if palliative measures are used, or will the condition progressively get worse? The problem is a difficult one, and yet of profound importance to the patient. Have we justification for saying that a prostate which has enlarged will go on progressively enlarging, and will it necessarily interfere more and more with complete emptying of the bladder. Even

if this be so, we know that in some cases the time intervening between the onset of early symptoms and the production of more severe symptoms varies through a wide range of time. Contrariwise, we also know some patients never manifest further symptoms, and the early symptoms disappear, the patient in effect remaining quite fit and in good health.

I have no doubt that if certain postulates could be laid down affirmatively in such cases the answer to my question would be "Yes," but can we answer the following questions affirmatively :—

(1) Is enlargement of the prostate necessarily progressive?
(2) Once symptoms, however slight, begin, do they necessarily worsen?
(3) Can the prostate be safely removed in otherwise healthy persons?

I do not believe progressive enlargement necessarily occurs even in the majority of cases. Early symptoms may entirely subside and no further symptoms develop. We cannot say that prostatectomy can be safely performed. It is a major operation, and is a definitely serious procedure to undertake. Some one writing the other day spoke of preventive surgery, but that cannot be applied to the prostate. If we have to deal with an adenoma or cyst of the mamma we advise removal, for one reason because it may later become malignant. Now while I quite recognise the risk of carcinoma arising in the prostate and in patients seeking advice for prostatic symptoms, my experience is that one in six or thereby suffers from malignant disease, and that this must be a factor for consideration, the difference in the case of the prostate as against the breast is the risk of a serious operation. The surgeon can remove an adenoma from the breast with almost complete impunity, but it is an entirely different matter, and the risk is infinitely greater when he performs a prostatectomy. A practical point also arises in connection with the operation; large and moderately large prostates are much more readily enucleated than small prostates, which have not, so to speak, shaken themselves free from their attachments.

In regard to this problem then, my opinion is that early operation is *not* justified, even when we have decided that the symptoms are due to prostatic enlargement. We should first try palliative means and watch the patient. From time to time

we should consider the case, bearing in mind the insidiousness of its advance if and when it progresses.

The position is wholly different when we have to deal with a more advanced case, *i.e.*, one in which the symptoms are worse, and especially if they are accompanied by other well-recognised signs. Thus a man not necessarily older than the patient who consults us with early symptoms, although more frequently a man of sixty years or older, gives a history as follows: "For the past year I have had to rise two or three times at night, and the frequency seems increasing, the flow is delayed and the force of the stream markedly lessened. During the day I have rather precipitate calls, and occasionally a small quantity comes away involuntarily. There is no pain, and otherwise, so far as I know, my health is good." You examine the prostate per rectum—it is obviously a large prostate, smooth, elastic, and mobile. You go into his case and you find that his arteries are soft, the blood pressure is not high, the tongue is clean, and the urine not increased in quantity. Specific gravity, 1015; reaction acid; no albumen, etc. He is a good operation life, and you recommend prostatectomy. Naturally, if he has had retention, or an epididymitis, the need for operation is emphasised.

A third class of case is in a different category from the two I have already mentioned, viz., the patient who, apart from local urinary symptoms, is obviously suffering from the symptoms secondary to them—those usually referred to as due to backward pressure, although it is difficult to think that this completely explains or accounts for them. In this category we have a man seriously ill. The tongue is dry, he is anæmic and has no appetite for food, but is exceedingly thirsty. He is getting thinner, and the mere statement that he "is not half the man he was" is often far from a complete description of the change in his general condition. The prostate is enlarged, but in addition the bladder may be obviously distended. He merely gets rid of overflow, and the urine is much increased in daily amount, 100 to 120 ozs., specific gravity 1005. Obviously, something must be done to relieve the condition, and done quickly, if he is to improve, but the important question arises, can he stand an operation—how is this to be determined? Various methods are in use, but I believe the most valuable is investigation of the condition of the urine, the daily quantity, the specific gravity, and the actual daily amount of urea excreted,

together with a determination of his general condition—heart and lungs especially. Supplementary to this we may use dyes —phthalein in particular, and the urea-blood index. Even with the use of all these methods, we may fail to gauge the actual condition. In some patients a fatal result follows operation in spite of every precaution, and in spite of one or other of the methods used indicating that the kidneys are still capable of functioning to a sufficient extent for operation to be carried out. There is no sufficiently reliable guide to determine success, although I believe we may usually readily enough determine in some cases that operation if undertaken will prove fatal. Can we in such cases so improve the condition of the patient that he will be able to have an operation safely carried out. I think we can only judge by the result produced by suitable treatment. The main endeavour is to relieve the so-called backward pressure, and this is done either by catheterisation two or three times daily for some days, or even weeks, or by draining through a cystostomy. I prefer the former, because I have seen patients die in twenty-four or forty-eight hours after a simple cystostomy. The kidneys simply ceasing to function after the bladder has been opened. In some cases after preliminary treatment by catheterisation a cystostomy can be done, and at a later period prostatectomy may be justifiable.

Up to this point, I have not referred to cases in which sepsis is present, but I think these cases only add additional weight to the need for operation. The sepsis *per se* from the operative point of view does not add, in my opinion, to the risk of operation. These patients seem to be to a certain extent immune, and stand operation better than cases in which the urine is apparently sterile. I am always very anxious about a patient who has an over-distended bladder of long standing, in which the only symptom in effect may be frequency and dribbling due to an overflow. In such a case, the symptoms are obviously due to defective kidney function, indicated especially by a large increase in the daily amount of urine and by the urine being of a low specific gravity. Catheterisation in these cases is a source of much anxiety, and must be carried out with special precautions to prevent infection. The bladder should not be completely emptied at first. A much more dangerous case is a patient with a markedly over-distended bladder without sepsis, in which the bladder-wall has lost all contractile power, and in which the distended bladder has

extended in every direction and is thinned out. When opened, it merely collapses and does not contract. In such a case, we know that the kidneys are very frequently much damaged and sometimes in such cases we have a very definite contra-indication to operation in the general condition of the patient. He is anæmic, has a dry tongue, is losing weight, circulation poor, and at night he has a slight tendency to wander. The urine, 100 to 120 ozs. daily—specific gravity 1005. Nothing will improve this man's condition, except relief of distention of the bladder. We recognise the risks, but it is justifiable to run them—what is the best thing to do? I think we should give urotropine for three or four days, and then with every precaution; catheterise regularly, and see whether kidney function improves. In some you must have a fatal termination—in others you can later carry out a permanent cystostomy—in others later, the patient having definitely improved, a prostatectomy can be carried out. To sum up this section of my subject I would say:—

(1) Early operation in Class 1 is not justifiable.

(2) In Class 2 operation is definitely indicated and is likely to be followed by success.

(3) In Class 3 operation is indicated, but it is only justifiable when we have determined that the patient's kidneys can functionate satisfactorily, and it is often necessary in these to use preliminary catheterisation for some time.

I now pass to the operation of prostatectomy itself. I prefer the suprapubic route in all cases where it is proposed to remove the prostate.

Choice of method.—It is natural that success in the circumstances I have shortly referred to must depend on other factors than the condition of the patient, viz., (1) preparatory treatment; (2) method of operation; and (3) post-operative treatment. I can dismiss preparatory treatment by referring to what I have already said, with this addition that just as in preparation for any other operative procedure, everything must be done to have the patient in the most favourable condition possible for operation. We must particularly note the renal condition, but in prostatic cases, just as in any other department of surgery, the surgeon must get his patient into as fit a condition as possible before undertaking operation. There is nothing

mysterious about it. A broken-down old man, a bad subject for operation, won't recover because it is his prostate that is being removed, any more than if he were undergoing an operation for any other cause. The anæsthetic is important, and while open ether is indicated in some cases, nitrous oxide and oxygen in others, the anæsthetic to use is determined simply on general principles. Spinal anæsthesia I have used with success, but it is only very occasionally needed. The patient may have the head and chest a little lower than the pelvis during operation, and he should be well under the anæsthetic. The bladder is sufficiently distended to present above the pubes, and I use a vertical incision and open the bladder close to the symphysis. Maissoneuve said: "The English say, 'Time is money'—to the surgeon, Time is life," and I believe in rapid operating, but it is not always necessary to do the operation in the minimum of time, and certainly the actual removal of the prostate should be carefully carried out. I do not think that in a moderately enlarged adenomatous prostate it is in the least necessary to see what we are doing. The finger enables us to do all we want. Bleeding is generally easily arrested by moulding the margins of the prostatic capsule, just as a dentist moulds the gum after an extraction. If the bleeding seems excessive, pressure can be used for a time, and later the use of hot water to wash out the bladder, or, if need be, we may pack the cavity from which the prostate has been removed, withdrawing the packing in forty-eight hours. To remove the prostate: I prefer to get down to the capsule through the mucous membrane at the opened-out portion of the urethra, or through the mucous membrane over the most prominent part of the projection into the bladder. Usually in the adenomatous prostate there is no difficulty in the enucleation, but in some cases there is some effort needed to separate it from the anterior or inferior surface. In a case where the prostate is more fibrous, or shall we say a fibrous prostate, enucleation is not so easy, and may be very difficult, but it must be the experience of all surgeons that frequently the prostate can be got out in a very perfect manner, and the case runs a perfectly normal course. In such cases of fibrous prostate, it is remarkable, I think, that stricture does not result. The condition seems just what should produce a fibrous stenosis at the neck of the bladder, analogous to the cicatricial stenosis which is occasionally met with in those cases of

"prostatism" that are liable to be mistaken for enlargement of the prostate.

Is the suprapubic route the route of choice, or should the surgeon select the perineal route? The method adopted should be that followed by the smallest mortality, always provided it gives an equally good result. I think the battle of the routes has been fought, and the majority of surgeons in America, as well as in Europe are in favour of the suprapubic. I advocate the suprapubic for the following reasons: (1) we can gauge the bladder condition better and deal with anything we find; (2) in patients who are bad subjects for operation, the prostate can be removed more quickly, and shock, I think, is less. The risks of urinary fistula or of incontinence are less. What arguments are used by the advocates of the perineal route? It is stated that the patient can be *out of bed sooner*, and that this is advantageous, particularly in old people, as it lessens the risk of pulmonary trouble. Is this any better than your patient sitting up in bed? I doubt if it is as good. That *drainage* is better I disagree Drainage with a suction apparatus is perfect, if properly carried out. What happens when the bladder is opened? It contracts and the urine is carried off as quickly as it is passed into the bladder. I believe in a tube in the bladder through the suprapubic wound, and that gentle washing out through it should be used once or twice daily. I do not approve of washing out through a catheter per urethram, unless it is put in at the operation. It may disturb the clot in the cavity from which the prostate has been removed. It should not be done until the tenth day at the earliest, I think.

Thomson Walker has recently advocated that the operation should be done with the prostate so exposed that we can see what we are doing. Two reasons for this suggestion may be urged, (1) that any bleeding from the torn capsule can be arrested, and (2) that all risk of tags being left behind which might later interfere with micturition can be removed with certainty. Fullarton of Belfast has also pointed out that in some cases the latter occurs, and requires further operation. I see no reason why this open method should not be adopted, in any case where there is excessive bleeding, or in which the capsule is irregularly torn; but as a routine, I do not think it is needed, and the extra time required for its performance in old, feeble patients, already bad operative lives, I think certainly

increases the risk. Further, the bleeding is, in my opinion, much greater from veins than arteries, and pressure can satisfactorily arrest it. The hæmorrhage, I fear, is reactionary, and this I think is venous, not arterial.

The results of prostatectomy are excellent, the mortality in early cases is very small, but in the late cases where the patients are broken down it is much larger. This is specially seen in hospital practice. The obvious moral to draw being that we must try to educate doctors to send their cases earlier, but certainly to induce patients to seek advice as soon as symptoms are manifested, from which time such cases should be observed, and whenever, if ever, they are definitely progressing in spite of treatment operation should be advised.

Discussion.

Mr Miles agreed that the prostate did not invariably continue to increase in size to the extent of causing serious symptoms, and deprecated operative interference in the early stages of the condition. He favoured the suprapubic operation being done through an incision in the bladder sufficiently free to admit of the field of operation being seen. He commended the palliative measures advocated for early cases by Mr A. G. Miller in the Society many years ago, and referred to cases in which these had proved beneficial.

Dr John Orr stated his experience to be that, since the introduction of prostatectomy, the position as regards the management of prostatic cases was much improved. Formerly, no good alternative to catheter life could be recommended with anything like confidence, operations such as vasectomy having proved useless. He did not regard age *per se* as a factor in determining or contra-indicating operation, this being decided with reference to the actual physical condition of each patient separately considered. He had had cases operated upon with immediate and lasting benefit, ranging between the ages of 46 and 80, and was of opinion that the operation saved patients with enlarged prostate a large amount of misery.

Mr Henry Wade said that Sir David Wallace had directed the attention of the Society to the great importance of determining the necessity or otherwise for operative treatment in the patient who presented himself for examination and was found to be suffering from the earliest manifestations of simple prostatic hypertrophy. Unfortunately, no statistics appeared to be available showing its incidence and the frequency with which it might remain as a non-progressive disability, slight in degree and causing no serious

interference with the patient's health and vigour. As such statistics were not available, and as the harmful consequences that resulted from this disease, if allowed to progress to its later stages without treatment, were known to every surgeon, it appeared to him that the early case not only required most careful investigation at the time of the original examination, but also required to be frequently re-examined to determine whether it was increasing in severity, and if so, undoubtedly immediate operative treatment for its relief was indicated. Prior to the war, Mr Wade had in the course of an investigation studied the records of various public hospitals as regards the results following the operation of prostatectomy. Those of the Royal Infirmary were taken over a period of ten years and found to have a high mortality, a state of affairs that was found to be the rule in all general hospitals. Recently, he had again studied the records of the Royal Infirmary and found that during the last ten years 511 cases of prostatic disease had been treated, 406 of which were recorded as cases of prostatic hypertrophy; the average age of these was 66 years, and their average stay in hospital twenty-nine days. Only 208 of these were operated on, and the average stay in hospital thereafter of those that were cured was forty-three days. The mortality still remained high, although it had much diminished, the high mortality being in his opinion due to the fact that the hospital still received so many of its cases in the last stage of the disease with whom the outlook was almost hopeless from the first. For the relief of these cases, the operation of cystotomy was undoubtedly of value as a preliminary preparatory treatment to a subsequent prostatectomy. In many cases this cystotomy was, however, performed on patients who were critically ill, and this was borne out by the statistics, where out of 47, 31 were cured and 16 died, a mortality of 34 per cent. Mr Wade was also of the opinion that in the case of advanced prostatic hypertrophy, valuable information could be obtained as regards the state of the kidneys by estimating the blood urea content, and that these cases required the most careful and, frequently, prolonged pre-operative treatment before they could be rendered in a fit state for the performance of the operation of prostatectomy.

Dr F. K. Kerr, speaking from the point of view of the general practitioner, said it was to be regretted that the condition was painless and so insidious in onset, because the elderly men took it as a matter of course as a condition associated with advancing years, and did not seek medical advice for mere frequency of micturition.

Mr Scot Skirving said that if enlargement, once begun, was always progressive., removal of the prostate at the earliest possible moment, even if symptoms were very slight, would seem indicated. Against such a course, however, was the fact, referred to by Sir David, that

enucleation generally became much easier as prostates increased in size. Mr Skirving thought that many of the deaths usually credited to shock were hæmorrhage deaths.

Mr Wilkie thought that in both the paper and the discussion the element of infection as a cause of death after prostatectomy had been given too secondary a place. In the post-mortem room he had investigated a number of fatal cases, and had been impressed with the frequency with which there was found a pelvic cellulitis spreading from the space of Retzius and associated with the presence of a septic broncho-pneumonia. Following the practice of the Mayo clinic, he had therefore endeavoured to immunise patients before operation with preliminary doses of vaccine. The advantages of the two-stage operation in feeble or badly infected patients were undoubtedly great, partly, he thought, from the fact that infective cellulitis in the pelvis was minimised owing to the space of Retzius being lined by granulation tissue at the time of the severe and exacting second stage of the operation, but also from the fact that in this region, as elsewhere in the body, a preliminary operation appeared to set in motion natural protective forces which robbed the subsequent operation of much of its risk.

Dr Goodall said that while it could be readily understood that surgeons should be impressed by cases of prostatic disease occurring at an early age, he would like to hear the experience of insurance medical officers on the subject. He was inclined to think that advanced age was the most important factor, and that insurance officials regarded prostatic disease with some complacency. An insured life who died of prostatic disease might diminish profits but he seldom caused loss, and the insurance office was content that he had not died sooner of some less profitable disease.

The President (Sir Robert Philip), Professor Caird, Mr C. W. Cathcart, Dr Edwin Bramwell, Dr Keppie Paterson, and Mr J. W. Struthers also took part in the discussion, and Sir David Wallace replied.

PRIVATE BUSINESS

The following were elected Members of the Society:—Arthur Mills, M.D., 3 Clarendon Terrace, Dundee; W. St John Cogan, L.R.C.P.Ed., Etc., 8 Vanburgh Place, Leith.

The President made a report *re* proposed alteration of method of issuing the *Transactions* which, if approved, will necessitate an alteration in the Laws. The Report was unanimously approved.

Transactions of the Medico-Chirurgical Society of Edinburgh

SESSION CI.—1921-1922

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SPECIAL CLINICAL MEETING.*

Sir ROBERT PHILIP, *President, in the Chair.*

Demonstration.

Dr Chalmers Watson gave a demonstration of **the intestinal flora as revealed by the use of a new culture medium.** A Gram-stained film of fæces ordinarily reveals a very large flora of organisms of coccal and bacillary forms, both Gram negative (coliform) and Gram positive. Cultivation on the media in common use yields an abundant growth of *Bacillus coli* either alone or with a very small number of Gram positive organisms; this fact has led to the prevailing teaching that a vast number of the organisms normally present in the fæces are dead.

The media commonly employed for the investigation of the intestinal flora are broth and agar, including glucose agar and various combinations of agar with serum, blood, etc. The essential ingredient of all agar culture media is a meat extract.

Certain theoretical considerations suggested to the author that the numerous bacteria which are not revealed on culture are not dead, but the methods in common use failed to reveal their presence. The general correctness of this view appears justified by the results obtained from the use of a new culture medium, which consists essentially in a particular combination of milk and agar. (This culture medium is at the present time in process of standardisation.) It is believed that such a medium more nearly reproduces the nutritive conditions obtaining in the small and large intestine. It certainly yields a growth widely different from that obtained by the methods usually relied upon. A smear from this culture uniformly reproduces a picture which approximates in its characters to the original smear.

From the point of view of our present knowledge of the bacteriology of the intestinal tract, a special point of interest is the revelation of the considerable proportion of streptococci present. The significance and the clinical value of the facts observed necessitate further investigation.

Exhibition of Patients.

Medical Patients.

Dr Robert A. Fleming showed—(1) a patient suffering from **lympho-sarcoma of the neck.** J. S., æt. 71, duration ten weeks. Began on left side of neck with "boil," which did not point. Large mass of glands matted but not adherent to skin, pushing larynx to right

* Held in the Royal Infirmary, 16th November 1921.

side. Little or no interference with œsophagus or trachea. Glandular masses extend down under left clavicle and left side of manubrium sterni. Secondary but discrete growths in both axillæ, both groins (especially left side), and down line of femoral lymphatics. Leucocyte count 11,000; no distinctive increase of any cell.

(2) A case of **splenic anæmia** with secondary cirrhosis of liver and ascites (Banti's disease). R. S., male, æt. 22, recommended by Dr Seal, duration 17 years; and ascites since August 1921. Illness dates from attack of measles at age of 5. He has been able to work intermittently as a printer's apprentice until summer 1921. The spleen is greatly enlarged, freely movable, and there is no evidence of recent or old perisplenitis. The liver is enlarged, surface and edge definitely nodular, and extremely hard. Ascites filled almost whole abdominal cavity when patient was admitted, but has gradually diminished in amount without tapping. It can only be made out at present by examination in the genu-pectoral position. Patient before admission and during most of his "attacks" complained of abdominal pain in region of umbilicus. There has been no pyrexia since admission, but he states that the "attacks" are associated with fever, especially at night; in fact abdominal pain and fever were the chief features of an attack. There was a slight tinge of jaundice on admission, with a trace of bile in the urine. Blood count: there is a chlorotic type of anæmia; red cells 3,000,000 to 3,500,000; hæmoglobin, 50 per cent.; and leucocytes, 2000. No important change in differential count of leucocytes has been noted. The tint of skin is very suggestive of the Gaucher type of splenomegaly, but the cirrhotic liver rules out this diagnosis. In preference to splenectomy the patient is to be treated with radium applied to the spleen.

Dr Rainy showed—the case of a boy, æt. 17, who exhibited the earlier symptoms of **Friedreich's ataxia**. The most prominent symptoms were horizontal nystagmus, choreiform movements of the head, absence of knee-jerks, and the occurrence of Babinski's sign. There was also typical bilateral pes cavus. The history gave some evidence of static ataxia, but this had not been apparent during his stay in hospital, and ordinary signs of ataxia were wanting. A brother, one year younger, had recently begun to give evidence of a similar malady, but in his case most of the symptoms were only slightly marked. He had, however, a very similar tendency to nystagmus, and his knee-jerks could not be elicited. A younger brother appeared healthy.

A very interesting fact in the family history is that his mother, his maternal grandmother, and her mother (*i.e.*, his great-grandmother) all suffered from nystagmus, but no further symptoms developed in their cases. The mother came to hospital, and the presence, in her case,

of well-marked horizontal nystagmus was readily identified. No opportunity of confirming the occurrence of the symptoms in the two older generations was possible, but there was no reason to doubt the truth of the statement.

Dr Edwin Bramwell showed—a case of **infantilism associated with diarrhœa.** W. R., a male, aged 22. *History.*—The patient's growth is said to have been arrested between the ages of 13 and 14; about the same time diarrhœa commenced (2 to 4 stools a day), and has persisted since. The patient states that he was treated with pancreatin regularly between the ages of 17 and 21; that he grew from ½ to 1 in. during this period, and that after commencing this treatment he thinks the motions became less frequent, though never formed. For eighteen months he has been troubled with giddiness, throbbing occipital headache at times, and occasional vomiting independent of food. Previous health good, nothing being noted until between 13 and 14 years of age. Family history unimportant.

Present State.—Appearance that of a boy of 14 or 15. Height 4 ft. 8¾ in., weight 5 st. 12 lb. Well-proportioned, though head relatively rather large (not typically hydrocephalic); muscularity poor; genitalia decidedly infantile; face devoid of hair, while pubic and axillary hair is sparse, and has not increased since 14 or 15 years of age; voice partly broken; epiphyses at elbows and knees have not yet joined; intelligence very good, and quite up to that of a man of 18.

No signs of rickets, tubercle (von Pirquet positive), or syphilis (Wassermann negative).

Tongue normal. Appetite poor. Abdominal discomfort associated with flatulence at times. Since the age of 15 he states that he has noted that fatty foods produce nausea, and aggravate the diarrhœa. Stools (1 or 2 daily) ill-formed, pale, slimy, and slight increase of fats while taking ordinary hospital diet. Total fat = 13.66 per cent. of dried stool. Fat partition; neutral fat = 90.23 per cent.; fatty acids and soaps = 9.77 per cent. (Report from Biochemical Laboratory.) The pancreas is secreting, since iodine reaction is obtained in the saliva one hour, and in the urine two hours, after taking a Sahli's capsule containing 2 grains of iodoform. No polyuria, no albumen, but an occasional trace of sugar in the urine. Sugar tolerance is lowered, as shown by the fact that after the ingestion of 50 grams of glucose at 8.30 A.M., there being no sugar in the specimen of urine passed previously, it was found that the urine contained .74 grains of sugar per oz. at 9.30, .91 at 10.30, and .48 at 11.30, while at 3 P.M. the urine was free from sugar. Blood sugar estimated by Dr Murray Lyon (Benedict's method) shows some increase, viz.:—Fasting level = .129 per cent.; following the ingestion of 90 grams of glucose, the blood sugar after 30 minutes = .263 per cent.; after 60 minutes = .377 per cent.;

after 90 minutes = .282 per cent.; after 150 minutes = .156 per cent. No urine was passed during the period of examination. Abdomen not unduly prominent. Lower border of stomach on percussion 1 in. below umbilicus. Splashing obtained two hours after a meal. Radiogram shows a j-shaped stomach (infantile type), no enlargement of colon, but the hepatic flexure is low, and there is a pronounced degree of visceral ptosis. The liver and spleen are of normal size, and no enlarged glands are palpable.

Heart and lungs normal; radial artery not thickened. Blood pressure, systolic = 104, diastolic = 88.

The blood shows, R.B.C. 6,310,000; W.B C. 6800; Hb. 80 per cent.; C.I. .64. Blood film shows no abnormalities. Differential count—polymorphs 70 per cent., small lymphocytes 20 per cent., large lymphocytes 9 per cent., eosinophiles 1 per cent.

Radiograms showed no enlargement of sella turcica. There is no change in the fundus oculi and no defect of the visual fields (Dr H. M. Traquair). No objective signs of derangement of the nervous system detected apart from persistent fine lateral nystagmus equally marked on deviation of the eyes to either side.

Bacteriological Examination of the Stools.—The patient was at the time taking a full hospital diet with no excess of sugar or milk. "No amœbæ or eggs were found and no dysentery bacilli isolated. The flora as a whole is definitely different from that of a normal adult; it is much more simple, contains few putrefactive organisms, and bacilli of the 'acid tolerant' group are predominant. It thus closely resembles the flora of a young child on a pure milk diet, though the appearance could also be produced by feeding older children or even young adults with large quantities of glucose or lactose, or by feeding them with living bacilli of the 'acid tolerant' group." (W. R. Logan.)

Dr Charles M'Neil showed—(1) a case of **chronic rheumatic endocarditis, with subcutaneous fibroid nodules.** The patient, a boy æt. 11, had his first attack of rheumatic fever in 1913, and has had numerous subsequent attacks of subacute inflammation of the joints. A mitral cardiac lesion was found in 1915, and has remained since, being now associated with definite enlargement of the heart. There were frequent attacks of sore throat (tonsillitis) up to 1917, when enlarged tonsils were removed. During 1917 and 1918 there were three attacks of chorea. In 1920 he developed acute pericarditis and was dangerously ill. Rheumatic subcutaneous nodules were looked for from the outset; they were first observed in the summer of 1921, and on the present occasion were demonstrated on the elbows and knees, of large size, but not numerous.

(2) A case of **paralysis of left facial nerve and of the right upper arm**, probably due to infantile paralysis (ponto-spinal type).

An example of "crossed" paralysis in a little boy, æt. $1\frac{10}{12}$ years, suddenly developing after three days of stupor and fever ten weeks ago. Paresis of the left side of the face and of the right upper arm are still evident. The fact of the paralysis of each part being of the flaccid and wasting type, pointed to the existence of two separate lesions, in the pons, and in the cervical enlargement of the spinal cord, and with the other clinical phenomena, supported a diagnosis of polio-myelo-encephalitis. There was a simultaneous occurrence of similar illness in a brother and sister, who both showed marked stupor and fever for three days. The sister developed thereafter a marked weakness of the back, and remained in bed, unable to sit up, for three weeks. The brother showed no paralysis. These other simultaneous illnesses throw doubt upon the etiology of the condition. The children had eaten rowan berries on the morning of their illnesses, which were attributed by the mother to this; but the absence of any symptoms of gastro-intestinal irritation would seem to exclude the possibility of some vegetable poison that had been swallowed.

Dr N. S. Carmichael showed—a case of **scleroderma**. Boy, æt. 7 years. Seven months ago his mother noticed his fingers becoming "curled up" and his wrist flexed, and a patch of discoloured skin on inner aspect right arm. Four months later she noticed patches of discoloration of the skin over the abdomen and chest.

Present State.—Patches of glossy ivory coloured skin, thickened and leathery over the chest and abdomen; some of them with a violet border. Over the inner aspect of both upper arms there are bands of similar character. Over flexor aspect of right wrist the skin is tightly stretched. The underlying tissues are atrophied and contracted with resulting flexion of the wrist and fingers, and partial fixation of the wrist joint.

Etiology.—History of diphtheria a year ago followed by weakness of the legs. No history or signs of rheumatism. No evident signs of impaired thyroid function.

Dr Watson-Wemyss showed—a case of **granular contracted kidney**. A girl, æt. 9, was admitted to Leith Hospital, on account of severe headaches and vomiting of three or four months' duration. She was quite bright and intelligent. There was a history of severe rickets and a double osteotomy had been performed for genu varum. She had also suffered much from bronchial catarrh, and had had a mild attack of diphtheria when three years old. For about three years before admission her mother had noticed polyuria and excessive thirst. The heart was enlarged and the second aortic sound was accentuated. The systolic blood-pressure on admission to hospital was 204 mm. H_E; estimated with a Riva Rocci instrument and a

12 cm. armlet. It was now constantly about 180 mm. H_E. Ophthalmoscopic examination revealed intense neuro-retinitis of albuminuric type in both eyes with large hæmorrhages. The left eye was now almost blind. The urine contained a moderate trace of albumen: no casts were at any time found. The renal function was tested by estimating the urinary diastase and the total non-protein nitrogen of the blood. The "d" value was 10 units. The total non-protein nitrogen was 36 mg. per cent. and the urea nitrogen 15.3 mg. per cent.

The child had had three or four generalised convulsions, no doubt uræmic in origin, and from time to time suffered from attacks of severe headache and vomiting, during which the hands often assumed the typical position of tetany.

Reference was made to a similar example of this very rare condition mentioned by Berkeley and Lee (*Amer. Journ. Dis. Child.*, 1917, xiii. 354), and also to the familial form of the disease described by Hellendall (*Arch. f. Kinderheilk.*, 1897, xxii., 61).

Dr A. Graham Ritchie showed—**three cases of congenital heart affections.** The three children—girl, æt 13, boy, æt. 11, and boy, æt. 7—are all undersized. All show the pronounced cyanosis known as morbus cœruleus, clubbed fingers and toes, dyspnœa, and erythræmia. The right side of the heart is markedly enlarged in all, and the apex beat displaced outwards, the precordia bulging. No other congenital deformity is present, and there is no history of antenatal maternal rheumatism.

In the case of the girl there exists a loud musical systolic bruit heard all over the precordium, of greatest intensity in the third interspace at the left border of the sternum. It is heard also in the interscapular region. The liver is greatly enlarged, and the tonsils frequently become enlarged and hæmorrhagic. The red-cell count is 8,500,000.

The elder boy shows well the distended venules on the chest wall. The first sound is reduplicated all over, and the second very accentuated at the base. The red-cell count is 9,000,000.

In the case of the younger boy there is a faint systolic bruit heard only up and down the left border of the sternum, with maximum intensity at the level of the third interspace. The red-cell count is as high as 11,000,000 with Hb 130 per cent. and high specific gravity. The cyanosis is most marked of the three, and the slightest exertion cannot be tolerated.

This striking hyperglobinæmia in the patients at rest would account largely for the cyanosis, the air pressure in the alveoli being unable to saturate the abnormal hæmoglobin content of the blood with oxygen.

From a study of the literature it is gathered that although congenital

malformation of the heart can be detected with certainty, post-mortem has frequently revealed another condition than was anticipated. The diagnosis of the above cases is therefore conjectured only, and the subsequent history is looked forward to with the greater interest. For permission to show the cases I have pleasure in thanking Sir James Affleck.

Surgical Patients.

Mr J. M. Graham showed—two patients after **prostatectomy** to illustrate the value of a preliminary suprapubic cystotomy in cases of enlarged prostate, in which the renal function and the general health have been seriously impaired by chronic retention and backward pressure: (1) A. M'L., æt. 71. Frequency of micturition and dribbling of urine had been present for thirteen months. The patient had, in a period of two months, lost over 2 stones in weight and his general condition was poor. The tongue was dry and he complained of thirst, weakness, and dribbling of urine. The bladder was visibly distended and reached to the umbilicus. Chronic cystitis was present and the specific gravity of the urine was 1006. Examination of the blood showed a high urea nitrogen concentration. A suprapubic drain was inserted into the bladder one week after admission, as it was noted that no improvement followed regular catheterisation. Following the cystotomy, which relieved the kidneys of the effects of backward pressure and permitted adequate treatment for the cystitis, the patient's health rapidly improved and prostatectomy was performed, with a satisfactory result after a period of twenty-four days' preliminary treatment.

The effect of suprapubic drainage on the renal function is shown by the following observations (by Dr Whitridge Davies) on the concentration of the blood urea:—

22.8.21. Blood Urea N. = 34 mgm. per cent. (normal 12 to 25 mgm. per cent.).
29.8.21. „ „ N. = 63 „ „
30.8.21. Suprapubic cystotomy.
7.9.21. Blood Urea N. = 35 mgm. per cent.
15.9.21. „ „ N. = 18 „ „
23.9.21. Prostatectomy.

The patient's physical condition is now excellent and urination is normal.

(2) A. M'G., æt. 86. This patient was shown to illustrate the late result of prostatectomy performed by the two-stage method three and a half years previously. Prostatic symptoms were first observed at the age of 73, and two years later retention of urine became complete. The catheter life was maintained for a period of eight years. In spite of the usual precautions cystitis soon developed and, frequently, the

catheter had to be passed seven or more times daily and several times at night to relieve him of discomfort. Some difficulty was latterly experienced in passing the catheter, and complete retention finally developed which could not be relieved owing to the presence of clots. On admission to the Deaconess Hospital on 24th March 1918 the bladder was found to be overdistended and the patient was in a state of collapse, semi-conscious, and with a pulse rate of 124. A suprapubic drain was inserted through a small incision made under local anæsthesia. After the first twenty-four hours, during which the patient was drowsy and in a critical state, his condition rapidly improved and became so satisfactory that prostatectomy was performed eleven days after the preliminary cystotomy. The patient has subsequently enjoyed good health with normal control of micturition.

Sir David Wallace showed—a case of **transplantation of the ureters into the pelvic colon.** A female patient, æt. 43, confined in July 1920. At that time there occurred fracture of the pelvis and such destruction of the soft parts in the perineum that the urethra and floor of the bladder were destroyed, the urine escaping directly on to the external surface. No plastic operation was possible, and on 29/9/21 the right ureter was transplanted into the pelvic colon, and on 21/10/21 the left was similarly dealt with. The urine now all comes per anum, the patient being able to retain from 12 to 15 oz. at a time. No bad symptoms have arisen and the patient is very comfortable.

Mr J. W. Dowden showed—(1) a case of **gluteal aneurysm.** Female, æt. 32. Had a bad fall in 1914 on buttocks and back of head. A year later she was troubled with "rheumatic" pains in left leg, which went on for about two years when she noticed throbbing in the left buttock when sitting, and also swelling which has been steadily increasing. She felt as if the swelling lifted her up with each pulsation when she was sitting. Left buttock markedly more prominent than right; numerous dilated veins. Pulsation to be felt, expansile in character. Nothing per rectum, but in the left lateral fornix just within reach of the finger a pulsating swelling could be felt. On auscultation a systolic murmur was heard nearly all over the buttock, most marked at the level of the great trochanter. A systolic murmur was also heard over the left femoral artery. Intra-abdominal ligature of the left internal iliac artery was carried out when compression of it was found to control the pulsation. An incision was made over the gluteal region, but owing to troublesome venous hæmorrhage was not persisted with. Cure, with a firm mass the size of an orange at the lower portion of the buttock.

(2) A **pulsatile angeioma.** Lad, æt. 18. First seen in 1913. History that some years before he had fallen and hit his forehead on

the left side and had had a lump since then which latterly began to increase in size. When seen the swelling was 1½ in. in diameter. It was pulsatile in character, and there were numerous enlarged arteries and veins about it. A number of ligatures were placed about the swelling but without improvement, and he did not return till 1916 when the pulsatile area was very much larger. This time a very extensive series of ligatures were placed all round the growth, but on his return in 1920 there was but little change. On this occasion a much more extensive operation was performed. The external carotid artery was clamped, and then a large U-shaped flap was turned down over the forehead taking the vascular area which was clipped away. The chief difficulty was about the orbital region, and he has now in 1921 returned with recurrence chiefly in the orbital region.

Mr George Chiene showed—a male patient, æt. 24, six years after removal of a **fibrous polypus of the base of the skull.** The symptoms prior to operation were naso-pharyngeal obstruction and epistaxis. He emphasised the importance of free access in operating on such cases, and drew attention to the very slight disfigurement present in the case shown. The operation which was performed under intra-tracheal anæsthesia, consisted in first tying the external carotid artery; then splitting the nose and lip, dividing the zygoma and frontal process of the malar bone through separate incisions and turning out the upper jaw, along with half the nose, without interfering with the palate. The tumour which was large but fairly well defined was then removed, the jaw, nose, and soft parts replaced and sutured in position.

Dr Douglas Guthrie showed—(1) a case of **cerebral abscess in a boy, æt. 6.** Five weeks ago this boy underwent operation for temporo-sphenoidal abscess. His right ear had been discharging since infancy, and on four occasions a mastoid abscess had been opened. Apparently no operation was performed on the bone, and although the mastoid wound healed, persistent discharge from the ear continued. For a month prior to admission to hospital this discharge had been profuse and fetid, and for a fortnight he had complained of headache and had vomited several times daily. He was dull and listless. Photophobia was evident. There was no mastoid tenderness, no paralyses of eyes or limbs, no nystagmus, and no optic neuritis. (Eyes examined by Dr Arthur Sinclair.) Radical mastoid operation was performed. A large mass of cholesteatoma filled the antrum and middle ear. No track of infection towards the brain was discovered, and the dura when exposed appeared healthy. Lumbar puncture revealed normal fluid, under tension. Despite the operation, the headache, dullness, and photophobia continued, and the wound was therefore reopened two days later. The dura was tense and bulging,

and the brain was therefore explored by a narrow bladed knife. At a depth of half an inch a large abscess was evacuated, and there was a profuse gush of thin fetid pus. The abscess was drained by rubber dam, and discharge continued for ten days. During this period his mental condition was peculiar. He was restless and noisy and complained of headaches, but his appetite was apparently ravenous and insatiable. He constantly called for food and was never satisfied. Those peculiar mental symptoms disappeared quite suddenly a fortnight after the abscess had been opened, when he took part with the other children in singing a nursery rhyme. Thereafter he appeared perfectly sane and intelligent. The wound is now healed and the bone cavity appears clean and healthy.

(2) **Nasal reconstruction for syphilitic deformity.** Between the ages of 9 and 16 this girl, now 18 years of age, suffered from nasal disease, apparently due to inherited syphilis, with the result that the nasal septum and columella were destroyed, and the bridge of the nose was sunken, causing a repulsive deformity. Wassermann was positive, and operation was deferred for several months, during which a course of neosalvarsan was given. Operation, 10/6/21, consisted in transplantation of a suitably shaped piece of costal cartilage so as to form a new nasal bridge. The operation is described in the December issue of the *Edinburgh Medical Journal.* The columella was reconstructed by two small skin flaps from the upper lip. The result has been very satisfactory.

Mr D. P. D. Wilkie showed—a case of **chronic duodenal ileus** complicated by gastric ulcer and treated by duodeno-jejunostomy. Miss C., æt. 54, had suffered since she was a young girl from "flatulent dyspepsia," with periodic bilious attacks. The latter consisted of severe headache and nausea lasting for a day and followed by bilious vomiting which gave complete relief.

In November 1920 she began to suffer from severe pain coming on within half an hour of taking food, and the vomiting which formerly had been occasional now occurred after every meal.

In April 1920 she was admitted to the Medical Wards of Leith Hospital. In spite of careful dieting the pain and vomiting continued and she steadily lost weight. A provisional diagnosis of carcinoma of the stomach was made and she was transferred for surgical treatment. Her weight before operation was 5 stones. At operation on 11th May the striking feature was the great dilatation of the first part of the duodenum which resembled a child's stomach; the second and third parts of the duodenum were also dilated as far as the point where the superior mesenteric vessels crossed it; thereafter the intestine was of normal size. To demonstrate the dilatation the better, a stomach-tube was passed and the stomach and duodenum were inflated with gas.

The great dilatation was more evident than before, and the compression of the duodenum by the mesenteric vessels was fully substantiated. The small intestines were all in the true pelvis and on raising them and relaxing the mesentery, gas passed at once into the duodeno-jejunal flexure. On the lesser curvature of the stomach, $2\frac{1}{4}$ in. from the pylorus, there was a chronic gastric ulcer.

As the duodenal obstruction appeared to be the primary condition, it was decided to leave the gastric ulcer alone and merely drain the duodenum by a duodeno-jejunostomy. Accordingly, a lateral anastomosis was done between the third part of the duodenum and the jejunum 7 in. from the duodeno-jejunal flexure.

From the day of operation the patient expressed herself as feeling a desire for food, and having an absence of the flatulence and nausea to which she had been accustomed for years. Her pain entirely disappeared and she rapidly gained in weight. Six months after operation she is able for a full day's work, has gained 2 stones 4 lb. in weight, and has no digestive symptoms.

Miss G. Herzfeld showed—(1) **two atypical cases of intussusception.** (*a*) Boy, æt. 17 months. Fourteen days' history of abdominal pain and vomiting; slight constipation, no passage of blood. Mass felt by Welfare doctor nine days before admission to hospital, who diagnosed abdominal tuberculosis. On admission, child looked ill; no marked distension—definite mass felt just above umbilicus. At operation irreducible ileo-cæcal intussusception found; apex enormously congested; no gangrene. Resection of ileo-cæcal region with end-to-end anastomosis of ileum and transverse colon. Uninterrupted recovery.

(*b*) Girl, æt. 8 years. Four days' history of vague abdominal pain with vomiting and constipation. Pain colicky in nature; slight streak of blood after enema had been given. On admission, tender mass in right iliac fossa. On laparotomy intussusception found in cæcum and ascending colon, apex formed by a Meckel's diverticulum, which could not be reduced. Resection of diverticulum and 4 in. of ileum—end-to-end anastomosis. Recovery.

(2) Case of **mesenteric cyst.** Girl, æt. 6 years. Complaint of intermittent pain for three months, swelling of abdomen, and loss of weight for two months. Cystic mass, size of adult head, in left half of abdomen and transgressing middle line—freely movable—painless. Colon displaced outwards—no connection with pelvis. On laparotomy, large mesenteric cyst about middle of small intestine. Resection of cyst and 9 in. of intestine and end-to-end anastomosis. Recovery. Cyst contained brownish, clear fluid—no evidence of chyle; wall consisted of dense fibrous tissue—with cholesterin crystals. Cyst probably lymphatic in origin.

Special Clinical Meeting

Mr Pirie Watson showed—(1) large "**whole-thickness-skin-graft,**" transplanted from the abdominal wall to right hand, after excision of scar tissue. Girl, æt. 17. Right hand crushed by a box-making machine in August 1920, causing laceration of the skin on dorsum of the hand and wrist, with comminution of the carpal bones. At the end of three months' in-patient treatment the wounds had healed with complete ankylosis of the wrist, and with a large contracted scar adherent to the extensor tendons of the fingers and thumb. The thumb was fixed alongside of the index; the fingers were stiff, semi-flexed at the interphalangeal joints, and hyperextended at the metacarpo-phalangeal joints. The wrist was ankylosed in good position, but there was no power of grasp, and no power of opposing thumb to fingers. The hand was useless. Ten months of out-patient treatment by massage had produced very little result.

Operation—16/9/21.—Excision of scar tissue, freeing of extensor tendons, manipulation of metacarpal and phalangeal joints, skin-graft.

A flap of skin about 4 in. by 3 in. was raised from the left abdominal wall, the base of the flap being lateral, and stitched to the hand so as to cover the area devoid of skin. The subcutaneous fat was included in the skin-graft to provide a suitable surface for tendon action. The thumb was placed in the opposed position, the abdominal wound repaired by undermining the skin, and the hand was retained in position against the abdominal wall by a plaster of Paris bandage, care being taken to keep the skin-graft relaxed. Fourteen days later—first dressing performed under general anæsthesia. The base of the graft was divided, the fixation of the graft to the hand and the repair of the abdominal wound completed.

The graft had well taken and bled freely when scratched.

16/11/21.—Considerable gain in movement; flexion of fingers almost complete in range at inter-phalangeal joints; opposition of thumb to index now possible; some power of grasp regained. The hand is already becoming of some use.

(2) **Stunted growth of left forearm and hand,** with superadded deformity from manus valga, and from extreme palmar-flexion at wrist. Man, æt. 32. Left forearm and hand dwarfed since infancy—cause probably congenital—in size resembling those of a young boy. Hand deviated to radial side, and acutely flexed at the radio-carpal joint. The ulna had outgrown the radius, the ulnar styloid being 1½ in. below the radial styloid. The lower end of the radius and bones of the carpus showed alteration in shape. Forearm semiprone, fingers and thumb fixed in extension, no power of grasp, hand useless, and deformity marked.

Operation—21/10/21.—Ulnar and radial incisions; lower end of ulna shortened by 1½ in.; obliquity of lower end of radius corrected;

removal of sufficiency of carpus to allow dorsiflexion of wrist. Wrist maintained in dorsiflexion by a palmar-hyperextension splint of aluminium.

Fourteen days later — first dressing, wounds healed, stitches removed, plaster of Paris bandage applied over hyperextension splint.

16/11/21.—Good position of wrist maintained, deformity lessened, already some improvement in movements of fingers and thumb.

Mr J. W. Struthers showed—(1) two men, æt. 44 and 23, after operation for **perforated duodenal ulcer.** One patient had had typical symptoms of duodenal ulcer for four months before perforation, but the other had only complained of some flatulence. Both ulcers were apparently of a chronic nature, as shown by the fibrosis round them. The cases were shown as examples of the great variation in symptoms which patients with duodenal ulcer present, and to emphasise the fact, which experience of a large number of cases of perforated ulcer shows, that duodenal ulcer may be, and often is, present for a long time without giving rise to any of the symptoms regarded as characteristic of that condition.

(2) A boy, æt. 16, from whom a **traumatic aneurysm** of the left radial artery had been removed. The aneurysm developed as a small swelling ten days after an aseptic punctured wound in the line of the left radial artery, 3 in. above the wrist joint. Six weeks after the injury the swelling had reached the size of a large pigeon's egg. Expansile pulsation and a bruit were present. The swelling was exposed, and it was found possible to shell it out completely from the surrounding tissues, so that it was removed entire with a section of the radial artery. On examination of the interior of the sac, a gap on the deep aspect of the artery was found about three-sixteenths of an inch long. The wall of the sac was examined microscopically and found to consist of laminated fibrous tissue without any trace of muscular coat.

DIAGNOSIS AND PROGNOSIS IN KIDNEY CASES BY TESTS FOR RENAL FUNCTION.*

By J. D. COMRIE, M.D., F.R.C.P.

THE presence of albumin in the urine was described by Bright in 1827 as a feature of disease in the kidneys, and its amount was for long used as a measure of the degree to which the kidneys are affected. This has, however, proved an insufficient guide, since albuminuria may occur without any kidney disease, and since, on the other hand, some of the severest cases of nephritis pass little albumin or occasionally none at all.

Various other tests for the functional power of the kidneys have therefore been proposed, and it is essential for any of these that it should firstly be accurate in result, and, in the second place, reasonably simple to perform.

Among the tests which have been proposed and again discarded, as not fulfilling one or both of these conditions, are the following. The co-efficient of Ambard is a figure much used in France, representing the relation between the amount of urea in the blood and the urea excreted daily in the urine; it has been objected to this test that it gives no additional information over the simple estimation of blood-urea,[1] that the rate of urea excretion is not dependent on its concentration in the blood and urine,[2] and that the method contains inherent fallacies.[3] The test-meal method of Mosenthal and Lewis[4] involves absolute regularity in meal-times, and the careful collection and measurement of the urine at stated periods, the test depending upon the varying relation, as regards amount and specific gravity, between the day and night urines, in health and in disease. Though simple in principle it is difficult to carry out with accuracy, and it has been shown by Boyd and Smith,[5] that some cases of advanced nephritis conform to the rule found in healthy persons. So that this test also does not possess a great measure of reliability. The diastase test[6] consists in the estimation of the amount of pancreatic starch-splitting ferment excreted in the urine; it has been found, however, that the amount of diastase excreted either by healthy persons or by nephritics varies within such wide limits that this test has also been generally abandoned.

The three tests with which the writer will deal in the

* Read 7th December 1921.

following remarks, and which after extended trial he believes to be the best are:—

(1) Amount of blood-urea (or, alternatively, an estimation of the non-protein nitrogen of the blood);
(2) Phenol-sulphone-phthalein test;
(3) Urinary urea concentration test.

(1) **Amount of Blood-Urea.**—This can be estimated quite conveniently and without elaborate apparatus in little over one hour by means of the soya bean "urease" ferment. It is fully described by MacLean and Russell,[6] and is carried out by taking a small quantity of blood (3 c.c.). This is incubated in a water-bath at about 40° C. for 15 minutes along with a small quantity of finely powdered soya bean, the urea being thus converted into carbonate of ammonia. The ammonia is liberated by addition of potassium carbonate to the tube containing the blood, and is subsequently drawn over by the action of a water-suction pump into 25 c.c. of centi-normal sulphuric acid, which after half an hour is titrated against 25 c.c. of centi-normal sodium hydrate. The difference found by titration corresponds to the amount of sulphuric acid already neutralised by the ammonia evolved from the urea in the blood. From this the amount of urea is simply calculated, every cubic centimetre of difference being equivalent to 10 mg. of urea per 100 c.c. of blood.

A few points of caution may be mentioned. The soya bean powder should be as fine as possible, and if kept too long may be found inert, but it retains its fermenting power for at least several months after being ground. The temperature of the water-bath should not be allowed to rise above 45° C. as the ferment is apt to be destroyed above that temperature. The blood must be examined within a few hours of being drawn, because under certain conditions ammonia-producing bodies quickly form and too high an estimation then results. The blood must be withdrawn before the administration of urea for the concentration test, since a considerable rise in blood-urea follows within two hours after the ingestion of the 15 grams of urea. The test is extremely delicate and reliable, however, and repeated examinations give practically identical results.

The normal blood-urea lies between 20 and 40 mg. per 100 c.c. Any estimation showing over 50 mg. may be taken

as indicating urea-retention and a decided degree of kidney inefficiency. When it is over 100 mg. the patient is usually a chronic invalid, the highest figures being obtained in cases of chronic parenchymatous Bright's disease. A blood-urea reading of over 200 mg. may be taken as an indication of impending death, though it may rise (*e.g.* Case 12, Table 2) to 371 mg. or higher; in another case (puerperal septicæmia showing fatty degeneration of the kidneys on post-mortem examination) it rose to 268 mg. just before death.

As a rule, the blood-urea changes slowly. In primary acute Bright's disease which is doing well it is not greatly raised, but in febrile diseases like pneumonia it may be raised temporarily considerably above the normal level. The negative evidence that it affords in combination with other tests is of great value. For example, one case with severe headaches and albuminuria, supposed at first to be nephritic, was found to have blood-urea 22 mg., phenolphthalein excretion 86 per cent., and urea concentration in urine 6 per cent.; the kidneys were therefore exonerated and the case was subsequently found to be one of enteric fever. Another case of headaches with albuminuria had blood-urea 31 mg., phenolphthalein excretion 90 per cent., and urea-concentration in urine 3·7 per cent.; and the albuminuria speedily disappeared, the case being one of neurasthenia with periodic albuminuria. In still another case of headaches, ultimately found to be occupational in origin, the blood-urea was found to be 21 mg., phenolphthalein excretion 90 per cent., and urea concentration in urine 2·5 per cent.

In cases where the disease of the kidney is moderate in degree, the blood-urea may be constantly well within the normal limits, and the prognostic indications must then be drawn from the other tests.

(2) **Phenol-sulphone-phthalein Test.**—This test, introduced by Rowntree and Geraghty about 1908, has been used by the writer extensively for the past ten years, both in civil practice and in the army, with uniformly satisfactory results as regards prognosis in kidney cases. It is carried out by injecting 1 c.c. of fluid containing ·006 gram of the pigment into the muscles of the back or limb. At the same time the patient drinks 600 c.c. (a tumblerful) of water, and empties his bladder. This urine is discarded. Thereafter at one hour and two hours precisely the patient again passes all the urine in his bladder and these two samples are tested for the amount of pigment

each contains. For this purpose the one-hour sample is rendered alkaline by 10 c.c. of 10 per cent. sodium hydrate solution, diluted to 1000 c.c. with water, and filtered to remove any phosphates precipitated by the alkali. A portion is placed in one container of a Duboscq colorimeter for comparison with a portion of fluid consisting of 1 c.c. of the testing fluid similarly diluted to 1000 c.c. and placed in the other container. The tints being matched by turning the screws of the containers up and down, the percentage of pigment excreted in the one-hour sample of urine is calculated as follows :—

$\frac{N \times 100}{U}$ = percentage of pigment excreted, where N is the height of the column of fluid in the container holding the standard dilution and U the height of the column of diluted urine. For example, if N stands at 20 mm. and U at 40 mm., then $20 \times 100 \div 40 = 50$ per cent. of the pigment excreted at the end of one hour.

The second-hour sample is treated in the same way, and should contain considerably less pigment than the first-hour sample. If the same amount or more pigment is excreted in the second hour, this indicates delay and a depressed renal efficiency. The amount excreted in the two hours added together should total at least 70 per cent. in health and may rise to 85 per cent. or even 90 per cent.

Other forms of colorimeter, such as that of Hellige, where a permanent standard is employed for comparison, are less satisfactory than the Duboscq, because their readings may be vitiated to the extent of 10 per cent. or more by the fact, as the writer has found, that the contents of the phenol-sulphonephthalein ampoule supplied by different makers vary considerably both in quality and in depth of red colour. This difference does not affect the reading of the Duboscq colorimeter, in which the standard used is the contents of an ampoule similar to that from which the patient receives the injection. Great care must be taken in carrying out this test that the patient receives exactly 1 c.c. of the fluid, that the bladder is completely emptied at the end of each hourly period, and that the injection is not made into œdematous tissue, from which absorption takes place slowly. It should be remembered that this test is really a criterion of the whole mechanism of absorption, circulation, and excretion of the pigment, not merely of the kidney activity. For this reason

the writer prefers the muscles of the arm for injection rather than those of the back, where œdema is apt to collect, especially in bed-patients with kidney or heart disease. An important possible fallacy should be mentioned. If the test be carried out while blood is still present in the urine the result will appear much too favourable. The blood may be removed by allowing the urine to sedimentise for twelve hours and then decanting it from the sediment, or by centrifuging. This fallacy should be borne in mind when testing a case of acute Bright's disease.

(3) **Urea Concentration Test.**—This test, introduced by MacLean and de Wesselow,[7] is very simply carried out. It depends on the fact that if 15 grams of urea be administered by the mouth to a healthy person it is quickly absorbed and excreted in the urine. In a specimen of urine passed two hours after the ingestion of this amount, there should be at least 2·5 per cent. of urea, while usually in a normal person the amount is 3·5 or 4 per cent., or in occasional cases more. If the proportion is only 2 per cent. or less it indicates a lessened power on the part of the kidney to concentrate urea, moderately severe cases of nephritis excreting only 1·5 per cent. or thereabout. While in severe cases, when uræmia is present. it may fall below 1 per cent.

The test is carried out by administering orally 15 grams of urea dissolved in water. (This amount, which is equivalent to the daily excretion on a low protein diet, does the patient no harm, and is not unpleasant to swallow. The writer's practice is to carry out the phenol-sulphone-phthalein and urea tests concurrently, the urea being dissolved in the 600 c.c. of water, which the patient drinks for the former test.) One hour after the urea has been administered the bladder is emptied and the specimen measured. At the end of the second hour, when the urea excretion is at its height, the bladder is again emptied, this specimen is measured, and the urea contained in it is estimated by the ordinary hypobromite process.

Gerrard's apparatus may be used for this purpose, in which 8 c.c. of nitrogen is the equivalent of 0·5 per cent. of urea. If the urea-tube of Doremus be employed, two of these tubes must be used in each estimation, for the reading on the lower part of the scale gives too low a result in urines which contain an approximately normal amount (3·5-4 per cent.) of urea; the 1 c.c. of urine, measured by the special pipette, is divided

between the two Doremus tubes containing hypobromite solution, and the readings of the nitrogen that collects in the two are added together.

The estimation of urea concentration and the phenol-sulphone-phthalein excretion do not always show absolute parallelism, but generally speaking they fluctuate together, and in cases where they disagree the two methods form a useful check upon one another.

Commentary on Tables.—Table I. (*see* p. 40).—Case 3 is a typical example of a subacute nephritis, with an exacerbation showing marked dropsy and albuminuria, high blood-pressure, headaches, etc.; the prognosis, with 52 mg. of blood urea, was at first somewhat doubtful, but the phenol-phthalein and urea concentration tests were good from the first and rapidly improved, along with a fall of blood-urea to 20 mg. The prognosis became therefore very good, and the patient left hospital after nine weeks apparently quite well. Case 6 is very similar. It will be noted in both of these cases that the fall in albumin corresponds to improvement in the functional tests. In Case 8 the phenol-sulphone-phthalein test does not reach the 70 level, and though the patient does her work as a student the prognosis is moderately good only. Case 10 is that of a patient whom I have had under treatment over ten years; she had severe optic neuritis in 1911; her survival may be associated with the good renal functional power she still possesses.

Table II. (*see* pp. 40, 41).—Case 1 and Case 2 are those of a son and father. In both the high blood-urea is to be noticed; in the son the urinary urea concentration power is good, but the phenol-sulphone-phthalein power only reaches the 50 level after three months' treatment; he will probably return to hospital worse this winter, though meantime he is back at school. In the case of the father the poor result of the function tests gave a very bad prognosis from the first, and he died seven months later; he had, however, very little œdema, and there was nothing in his general appearance to indicate a speedy demise. Case 12 shows similar poor function tests, but the symptoms were more urgent. In Case 13 both kidneys have been decapsulated; the patient is still under observation, but I cannot help giving a bad prognosis in view of the poor functional efficiency tests, though he is much relieved as regards dropsy and other general symptoms since the last operation. In Case 14 the tests indicate a prognosis for life of several years with care.

TABLE I.—*Parenchymatous Nephritis: Good Prognosis.*

Case.	Age, Sex.	Clinical Diagnosis.	Date.	S.B.P.	Amount of 24 hours' Urine.	Albuminuria.	Casts.	Blood Urea, mgr. per 100 c.c.	Phenol Sulphone Phthalein Test.	Urinary Urea.	Wassermann Reaction.	Clinical Result.
				MM.	C.C.	PER CENT.		MGR.	PER CENT.	PER CENT		
3	45 M.	Subacute Nephritis	24.4.21	180	1700	0·55	H, G	52	37, 32 = 69	2·5	–	In good health, fit for work.
			4.5.21	...	700	0·25	,,	...	38, 26 = 64	3·0		
			20.5.21	115	1600	0·01	,,	...	43, 28 = 71	3·0		
			19.6.21	115	1450	0	...	20	49, 37 = 86	3·6		
			2.7.21	115	...	Trace	None	...	41, 29 = 70	3·4		
6	44 M.	Subacute Nephritis	21.2.21	140	...	0·16	H	...	48, 8 = 56	1·5	–	Robust, fit for work.
			18 3.21	...	...	0·05	None	29	58, 27 = 85	4·0		
			30.3.21	...	...	0	,,	...	...	...		
8	17 F.	Subacute Nephritis (B. coli infn.)	18.6.21	130	...	0·04	H, G	26	40, 26 = 66	3·2	...	Fair health; persistent albuminuria 5 months later.
			1.7.21	130	...	Trace	None	...	...	...		
10	37 F.	Chronic Nephritis . (Optic Neuritis)	14.6.11	...	3700	0·50	E, G	...	...	...		Blind in 1911.
			18.5 21	160	1500	Trace	G	29	30, 40 = 70	2·7	–	Fairly healthy; active life; good vision 1921.

TABLE II.—*Parenchymatous Nephritis: Bad Prognosis.*

1	13 M.	Acute Nephritis .	2.4.21	...	570	0·04	B, E	63	40, 26 = *66	3·2	–	Became subacute; general health fair.
			11 4.21	115	1140	0·04	,,	41	60, 20 = *80	4·0		
			26.6.21	112	340	0·06	None	64	28, 22 = 50	4·0		
2	58 M.	Subacute Nephritis	9.3.21	242	2000	0·60	E, G, H	128	Trace	1·3	–	Chronic invalid; readmitted 16.8.21; died 3.11.21.
			4.4.21	204	1420	0·50	,,	167	,,	1·3		
			20.4.21	...	2000	0·50	,,	94	5	0·8		
			2.5.21	...	2000	0·30	,,	...	2	1·0		
			28.8.21	...	...	...	...	98	4, 5 = 9	1·4		
			8.10.21	...	...	...	...	...	0	1·4		

9	62 M	Chronic Nephritis .	4.7.21	122	1900	+	E, G, H	144	24, 25 = 49	2·3	–	Chronic invalid.
			16.7.21	120	1000	+	,,	136	32, 21 = 53	2·9		
12	49 F.	Chronic Nephritis .	18.4.21	140	570	0·15	G	349	Trace	0·8	–	Died of uræmia, 22.4.21
			20.4.21	...	120	+ + +	...	371	None	...		
13	35 M.	Chronic Nephritis . (+ Acute)	26.5.21	168	430	1·70	B, E	131	12, 13 = 25	2·3	–	Little better after 2 months ; R.K. decaps. 26.7.21; improved, attempted work ; L.K.decaps. 18.11.21; improved, but confined to bed.
			17.6.21	148	860	0·60	,,	134	5, 17 = 22	2·5		
			23.6.21	150	1150	0·40	,,	114	7, 13 = 20	2·0		
			4.7.21	162	1200	0·90	,,	73	12, 12 = 24	2·4		
			27.7.21	182	540	+ +	,,	87	21, 15 = 36	2·0		
			2.10.21	180	1950	0·50	E, G	30	40, 14 = *54	2·0		
			27.11.21	...	...	...	...	33	10, 7 = 17	1·2		
			7 12.21	180	2100	1·00	B, E, G	34	20, 12 = *32	1·4		
14	24 M.	Chronic Nephritis .	31.5.21	210	...	1·20	B, G, H	...	...	...	–	Moderate health ; fit for light work.
			18.6.21	182	900	0·70	,,	25	30, 25 = 55	2·2		
			26.6.21	172	1900	0·90	G, H	79	18, 17 = 35	2·0		
			9 7.21	138	1200	0·60	,,	...	31, 23 = 54	3·5		
			25.7.21	146	1450	0·35	...	33	26, 23 = 49	2·2		
			29.10.21	...	...	0·90	None	20	44, 25 = 69	2·8		

TABLE III.—*Interstitial Nephritis*

15	68 M.	Interstitial Nephritis	8 3 21	250	1200	0·60	G, H	54	0, 30 = 30	1·7	–	Fit for light work ; persistent headaches.
			3.4.21	230	1000	Trace	,,	...	0, 30 = 30	3·0		
			15.5.21	...	...	0	None	...	10, 42 = 52	...		
16	58 F.	Interstitial Nephritis	7.1.21	280	1800	+	G, H	...	...	...	–	Retinal hæmorrhages, 12.20 ; persistent headaches ; leads ordinary life with care.
			5.5.21	300	1600	Trace	,,	28	36, 30 = 66	2·3		
			1.6.21	240	1600	,,	,,	...	...	...		
			29.11.21	240	...	,,	...	...	...	...		
17	66 M.	Arterio-sclerotic Kidney	30.3.21	154	1300	Trace	None	37	25, 28 = 53	1·7	–	Aortic aneurysm ; chronic invalid
			4.4.21	150	1700	,,	,,	38	20, 33 = 53	1·0		
			1.5.21	140	1200	0	,,	...	24, 27 = 51	2·2		
18	84 M.	Arterio-sclerotic Kidney	9.4.21	220	1500	Trace	None	26	33, 36 = 69	1.5	–	Excellent health for age.
			15.4.21	200	1400	0	,,	...	...	...		

* Result too high owing to presence of blood.

TABLE III.—*Interstitial Nephritis*—continued.

Case.	Age, Sex.	Clinical Diagnosis.	Date.	S.B.P.	Amount of 24 hours' Urine.	Albuminuria.	Casts.	Blood Urea, mgr. per 100 c.c.	Phenol Sulphone Phthalein Test.	Urinary Urea.	Wassermann Reaction.	Clinical Result.
				MM.	C.C.	PER CENT.		MGR.	PER CENT.	PER CENT.		
30	38 M.	Early Interstitial Nephritis (?).	16.8.21 25.8.21	230 115	1600 1400	Occ. trace 0	H None	55 25	25, 27 = 52 33, 32 = 65	2·3 2·7	–	Fit for work.

TABLE IV.—*Cardiac Decompensation.*

21	31 F.	Cardiac Dilatation.	17.5.21 1 6.21	102 120	1200	Trace 0	None	24	36, 21 = 57	2·5	...	Recovery.
24	12 M.	Endocarditis, Mitral and Tricuspid	18.4.21	124	1200	0·02	H	21	42, 30 = 72	4·0	...	Great hypertrophy. Died heart failure; no œdema.
26	28 F.	Mitral Stenosis .	27.5.21	125	1200	Trace	G	28	40, 30 = 70	2·2	...	Recovery.
22	68 M.	Mitral Disease (Aur. fibrilln.) .	19 3.21 6.4.21	92	570 700	0·30 +	H	34	8, 8 = 16 27, 30 = 57	2·5 2·2	–	Died suddenly, 18.4.21.
23	61 M.	Mitral Disease (Aur. fibrilln.) .	21.3.21 6.4.21	110	850 430	+ +	B, E	61	20, 20 = 40 26, 30 = 56	2·0 3·2	–	Died, heart failure.
25	64 M.	Mitral Disease (Aur. fibrilln.) .	17.5.21 20.6.21	110 110	600	0·02	H, G	37	0, 16 = 16 6, 20 = 26	2·7 2·8	...	Chronic invalid.
27	30 F.	Mitral Disease (Aur. fibrilln.) .	14.3.21	110	...	+	H	44	10, 10 = 20	2·4	...	Chronic invalid.
29	47 M.	Aortic Disease .	20.6.21 11.7.21	128	1500 1000	Trace „	None	44	0, 20 = 20 23, 12 = 35	2·4 3·4	+	Much œdema; died 20.10.21.

Table III. (*see* pp. 41, 42).—The tendency of the blood-urea to be high, and of the phenolphthalein level to be about 50, is shown. In Case 18 there was apparently only a senile arterio-sclerosis with fair functional kidney power. Case 30 shows the characters of an early interstitial nephritis; with the response of kidney function to treatment the patient is probably good for many years.

Table IV. (*see* p. 42) shows generally in the first three cases the good functional kidney power of cardiac cases in which compensation is speedily established. In cases with bad compensation, *e.g.* in auricular fibrillation, the blood-urea is high, the phenol-phthalein test either fails to reach or at all events to pass much above the 50 level, while the urea concentration power is moderate. Probably some of the bad symptoms in cardiac decompensation are due to defective renal function.

Conclusions.—1. The combination of the three tests described gives reliable information as to the functional efficiency of the kidneys.

2. The blood-urea estimation is of a primary nature. If it rises above 50 mg. per 100 c.c. of blood, the condition is serious. If it is persistently over 100 mg. recovery is not likely and death will probably take place within a year. In uræmia it may exceed 200 or even 300 mg. before death. The blood-urea may, however, remain normal while a marked degree of renal impairment exists, and in such cases the immediate prognosis is generally good.

3. The blood-pressure shows no constant relation to the amount of blood-urea; though where blood-urea is permanently high the blood-pressure is usually raised.

4. The phenol-sulphone-phthalein test is, in the writer's opinion, the most valuable individual test. An excretion that takes place chiefly in the first hour, and that in two hours reaches over 70 per cent., gives a good prognosis so far as the kidney function is concerned. An excretion of 50 per cent. for two hours in either renal or cardiac cases is compatible with complete restoration of health. An excretion of about 30 per cent. is compatible with prolonged life, though on a low plane of vitality. When the excretion does not rise above 20 per cent. death within a year may be expected.

5. The urea concentration test is simple, harmless, and useful. A concentration over 3·5 indicates satisfactory renal

function; over 2 per cent. it is compatible with a fair degree of health; when it persists below 2 per cent. despite treatment it is unsatisfactory.

REFERENCES.—[1] Chace and Myers, *Journ. Amer. Med. Assn.*, 1916, No. 13, p. 929. [2] Addis and Watanabe, *Arch. Int. Med.*, 1917, p. 507. [3] Van Glyke and Cullen, *Journ. Biol. Chem.*, 1914, p. 211. [4] Mosenthal and Lewis, *Journ. Amer. Med. Assn.*, 1916, p. 133. [5] Boyd and Malcolm Smith, *Brit. Med. Journ.*, 1921, ii., p. 428. [6] MacLean and Russell, *The Lancet*, 1920, ii., pp. 1306, 1307. [7] MacLean and de Wesselow, *Brit. Journ. Exper. Path.*, 1920, i. p. 53.

Discussion.

Dr R. A. Fleming said that he had watched these tests being carried out, and knew most of the cases described. The phenol-sulphone-phthalein test was, in his opinion, the most valuable. A possible objection to the blood-urea test was, that it involved the withdrawal of blood, which might be disturbing to the patient: the test also took up a good deal of time. It was curious that in heart conditions the results of the tests seemed to favour a kidney affection; but it was probable that a proportion of the retained nitrogen was held up in the liver and other organs. In many of his cases he had found the results of these tests valuable, especially in encouraging perseverance in treatment.

Dr Whitridge Davies asked if any ill-effects had been noted to follow the administration of urea, for he had known a case where the intravenous injection of urea had caused hæmaturia. His results with soya bean meal had not been satisfactory, and he had found it necessary to use prolonged incubation to get constant results. High blood-urea need not always indicate a serious renal condition, *e.g.* in a girl of twelve with scarlatinal nephritis the high blood-urea was found to be due to an associated acidosis, and it fell rapidly after alkaline treatment. Much more work was required on the functional efficiency of the kidney; there was also the question of salt retention to be considered, as well as prostatic cases with excessive excretion of water and desiccation of the issues.

Dr W. T. Ritchie said that he had found the tests useful in cardio-renal cases, and especially the phthalein test, and he could recall cases where the result of the test had made the prognosis still more unfavourable. In a case of chronic headache, the blood-urea test had exonerated the kidney, and the diagnosis of the condition had been found in a positive Wassermann test of the cerebro-spinal fluid.

Dr Chalmers Watson said that two important discussions on this subject had taken place elsewhere within the past year. One introduced by Prof. M'Lean dealing with the results based on his experience of

these tests in over 15,000 cases. It seemed clear from the views there expressed that the appreciation of their clinical value was decidedly more qualified than a few years ago. Prof. M'Lean apparently considered that the urea concentration test was the most valuable; others with large experience of the various tests laid most reliance on the pigment test. In a recent discussion of a section of the Royal Society of Medicine, Mr Everidge—who introduced the discussion—spoke with the greatest approval of the pigment test, and in assessing its value he indicated that in 54 per cent. of his cases the test was "thought to be valuable because its results agreed with the results of other similar tests. In many cases the results were doubtful, and in 15 per cent. the results were quite misleading." In placing reliance on the test it seemed to the speaker that too great assumptions were made, and more especially it seemed to be assumed that the rôle of the liver, muscles, and other tissues in dealing with the urea and other substances employed in the test were negligible, and this appeared to the speaker to be doubtful. With regard to the urea concentration test, which, if reliable, would be especially valuable because of its extreme simplicity and the facility with which it could be carried out by the practitioner, the speaker had made a series of investigations in cases other than those that could be clinically labelled "nephritis." The wide variation in the results obtained in this inquiry rather confirmed him in his view as to the need for caution in drawing deductions with regard to the practical value of these tests, either in the diagnosis or prognosis of renal disease.

Mr J. W. Struthers asked for the precise indications of prognosis which these tests yielded beyond the ordinary clinical features of improvement, or the reverse. Did they give information which was not given by the ordinary general observation of the patient?

Dr J. D. Comrie, in reply, had seen no ill effects from the administration of urea, beyond an increase of headache in one case. The temperature of incubation of the blood with soya bean meal was important, and should not exceed 45° C.; also, the meal must be in a fine state of division. He had found the pigment test the most helpful; but in any case one test was not sufficient—a series was needed, one to control another. He was satisfied that these tests gave valuable information beyond that yielded by ordinary clinical observation.

Mr D. M. Greig gave a demonstration of certain features of the **Oxycephalic Skull**, illustrated by lantern slides from three clinical cases, and one skull.

PRIVATE BUSINESS.

The President read a Congratulatory Address received from the Edinburgh Obstetrical Society on the occasion of the Medico-Chirurgical Society attaining its Centenary.

The following were elected Members of the Society:—John Cormack Simpson, M.B., Ch.B., D.Ph.; Frederick W. K. Tough, F.R.C.S.E.; Hugh Richardson, D.S.O., M.D.; Malcolm Macnicol, M.A., M.D.; Mrs Mary H. Macnicol, L.R.C.P. & S.

The Treasurer presented his Financial Statement for the year 1920-21, which was adopted.

The President intimated that the agreement with the *Edinburgh Medical Journal* with regard to the publication of the *Transactions* of the Society had been completed.

The Senior Secretary tabled a motion on behalf of the Council relating to alterations in the Laws.

THE SIGNIFICANCE AND TREATMENT OF GLYCOSURIA.*

By HARRY RAINY, M.D., F.R.C.P.E.

In opening the discussion on the nature and outlook of glycosuria, perhaps the most important point to be emphasised is that a fuller knowledge of its causation has led to so great an advance in treatment that the figures presented in various statistical returns can leave no reasonable doubt in the mind of the greatly improved prospect for the patient.

In the recent *Diabetic Manual*, written by Joslin for the instruction of his patients, he gives a very striking paragraph on the altered outlook in the Massachusetts General Hospital. He shows that from 1824 to 1898 the percentage mortality during hospital residence was 27 per cent.; from 1898 to 1914, 28 per cent.; but that in 1914 the mortality dropped to 16 per cent., in 1915 to 12 per cent., in 1916 to 8 per cent., in 1917 to 6 per cent., and in 1918 to 4 per cent.

Of course, every one who has had much experience of statistical records knows how full of fallacy they are, both on account of the relatively small number of cases concerned in statistics of this sort, and also from the fact that a better medical education leads to earlier diagnosis and, consequently,

* Read 15th February 1922.

to an earlier admission to hospital where the cases stay for a shorter time, and so the deaths do not fall within the period of hospital residence. Still, making all allowance for these facts, the curve is striking, and the drop so regular and continuous, that one is forced to the conclusion that some really important factor is at work in producing the alteration.

If one accepts as the definition of diabetes that of a disease in which the normal utilisation of carbohydrates is impaired, with the result that glucose is excreted in the urine in recognisable amount, one must reckon with the fact that there are various other types of glycosuria which would fall within this definition; but from the clinical point of view it is wiser to accept Joslin's position that any patient who has a demonstrable quantity of sugar in the urine is suffering from diabetes mellitus, unless the contrary can be clearly proved.

Time does not allow of any lengthy retrospect of the history of the disease; those who desire details will find them in the works of Cantani, Cammidge, and others, whilst a short résumé up to date with a reference list to the literature is furnished by Allen. In the earlier periods there is no very definite evidence of recognition of the malady, but several of the writers of the first century of the present era note the existence of a disorder where the excretion of urine is greatly increased, and Aretæus of Cappadocia first gave the condition its present name. The disease was also mentioned by Celsus, Paulus Ægineta, Galen, and others, whilst references by oriental physicians have also been noted. Little advance, however, was made till the seventeenth century, when Willis called attention to the sweetness of the urine which suggested the presence in it of honey or sugar, and from that time onwards slow but steady advances were made in our knowledge of the condition.

Long before this, however, treatment of the disease, little though it was understood, seems to have been attempted, and, apart from medical treatises which deal with the subject, there is an interesting letter, written in 1374 by Boccaccio who was suffering from diabetes, to his friend Francescuolo da Brossaro, the son-in-law of Petrarch.* In this letter the following paragraphs occur:—

"But I must tell you that ten months ago, while I was lecturing in Florence on the *Commedia* of Dante, I was seized with illness, not so

* Toynbee, *Dante Studies*, p. 59, Oxford, 1921.

much of a dangerous nature, as long and wearisome. For four months past, at the entreaty of my friends, I have been in the hands, I will not say of physicians, but of quacks, who have not only increased my malady, but by doses and starvation have so upset my digestive organs, that I am reduced to a state of weakness hardly to be credited by any one who has not experienced it—my looks, however, tell their own tale to every one who sets eyes on me.

"Poor wretch that I am, you would find me sadly changed from what I was when you saw me in Venice! The skin of my body, once plump enough, is all shrivelled up, my colour has gone, my eyes are dim, and my hands tremble, while my knees are so unsteady, that so far from attempting to cross the Apennines, I could only just drag myself out of Florence with the help of friends to my farm here at Certaldo, where I remain, more dead than alive, torn with anxiety, and wasting away in idleness, not knowing what to do with myself, my sole hope of a cure being in the grace of God, who is able to overcome all diseases."

It is perhaps interesting for members of an Edinburgh Medical Society to note that Cullen included diabetes in his *First Lines of the Practice of Physic* in 1784, from which the following extract may be quoted:—

"As I have already said, I think it probable, that in most cases the proximate cause of this disease is some fault in the assimilatory powers, or in those employed in converting alimentary matters into the proper animal fluids. This I formerly hinted to Dr Dobson, and it has been prosecuted and published by him; but I must own that it is a theory embarrassed with some difficulties which I cannot at present very well remove.

"The proximate cause of diabetes being so little known or ascertained, I cannot propose any rational method of cure in the disease. From the testimony of several authors, I believe that the disease has been cured, but I believe also, that this has seldom happened; and when the disease has been cured, I doubt much if it was effected by the several remedies to which these cures have been ascribed."

In 1796 John Rollo's treatment of diabetes by dietetic rules first came into notice, and although the diet was very far removed from our present practice it may be said to mark a new beginning in the methods of treatment, and its employment was apparently followed by a degree of success which the procedure recommended barely justified. It marked, however, a certain effort to escape from the tyranny of drug therapy which had previously too largely monopolised the attention of physicians.

Modern knowledge, however, begins to advance with the

work of Claude Bernard, who discovered glycogen and the glycogenic function of the liver, and who also described the glycosuria which is produced by puncture of the floor of the fourth ventricle.

On the clinical side, the work of Bouchardat led to the more rational dietetic treatment of the disease, and he must be credited with the inauguration of occasional fast days to control glycosuria. This was about the year 1851. At a later date (1875) he suggested a connection between the pancreas and glycosuria, which has subsequently proved so fruitful.

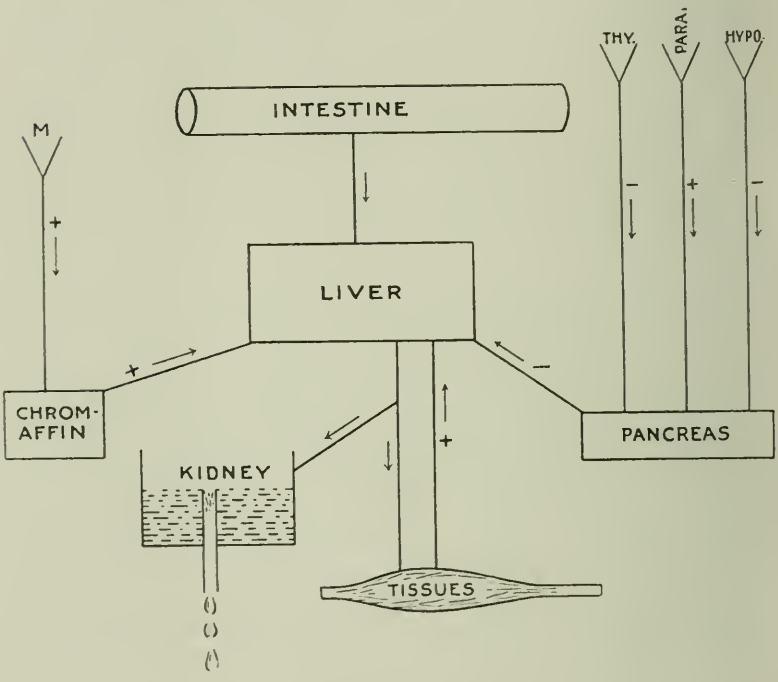
In 1857, Petters identified acetone in the urine of patients suffering from diabetic coma, and in this country Pavy began his investigations into glycosuria. Whilst many of his views have proved to be inadequately supported, the work which he carried on for over half a century, from 1853 to 1911, has materially increased our knowledge on many points of the disease.

The first study of the respiratory metabolism of the diabetic patient is attributable to von Pettenkofer and Voit, in 1851, whilst Ebstein also directed much attention to the physiological chemistry of the disease. In 1874 Kussmaul gave a detailed description of diabetic coma, Cantani developed more fully the dietetic treatment of the disease, and work of great importance was performed by Lancereaux, von Frerichs, Kulz, von Mering, Klemperer, Naunyn, Neuenahr, Minkowski, and Lenné; whilst of the present generation special mention must be made of von Noorden, Guelpa, and Cammidge in Europe, and of Allen, Macleod, Joslin, Opie, Benedict, and Van Slyke in America.

Much notice has lately been taken of the dietetic work of Guelpa of Paris. Basing his treatment on the view that in the most varied types of disease, in the absence of emaciation, an accumulation of products of fermentation—(toxines and the debris of poisoned tissues)—occurs, he seeks to promote their elimination in order to further the return to health. He therefore advocates three-day fasts on repeated occasions with a daily bottle of hot Hunyadi Janos to clear the alimentary tract. The fasts recur at gradually lengthening intervals during which are given milk, green vegetables, etc. In 1911 he added instructions regarding the treatment of acidosis which he did not mention in his earlier papers. He thus anticipated in many of its details the so-called "Allen treatment," and, although his explanation of the way in which the treatment works is defective,

he deserves the greatest credit for directing or redirecting attention to the primary importance of under-nutrition, and to this extent he anticipates and in fact initiates the principles of that school of investigators which has now become dominant.

Time, however, renders it impossible to deal historically in any detail with the individual contributions of workers since the middle of last century.



The result of all these investigations has been to lay stress on the fact that glycosuria may arise in a great variety of conditions. A diagram, founded upon one which so far as I know was first suggested by von Noorden, may help to demonstrate this and also to show their interrelation.

Here we see how glycogen mobilisation is increased in the liver by the stimulation of the chromaffin glands and the call of the muscles, whilst it is checked by pancreatic inhibitory influences. It is also shown how these guards are themselves under control and how the kidney, in virtue of its liminal action, only allows the escape of sugar when the concentration in the blood is too great. It does not show how the kidney is not a passive agent,

but necessarily does work in concentrating the urinary sugar far above the highest possible limit in the blood; nor does it indicate that the thyroid and hypophysis may rather act on the nervous system than influence the pancreas directly.

A matter of considerable importance in any studies of diabetes is the clear differentiation of different types of glycosuria, and in order to achieve this—to which we shall presently return—it is of the first importance to be able to estimate with considerable accuracy the sugar content of the blood. This can be performed by various methods, whose suitability depends on the frequency with which the condition being examined for demands extraction of blood. Ordinarily, the colorimetric method is sufficient, but where blood has to be taken at short intervals it is most desirable to adopt some process in which a much smaller quantity is necessary, so that it can be repeatedly taken from the patient without much annoyance. Of chemical methods there are now a large number, and in a paper by Miss Hawick and myself, which was read before the Royal Society of Edinburgh in May 1916, we discussed the relative values of (1) Rona and Michaelis' method for protein precipitation, combined with Bertrand's sugar estimation; (2) Maclean's recent methods; and (3) the "micro-method" of Ivar Bang, and gave our reasons for preferring the last of these, provided certain minor modifications were made to increase the accuracy and certainty of the results. In this method the chief difficulty is that unless great attention is paid to details of technique, errors of considerable amount may enter into the estimations. By following the procedure detailed in our communication most of these errors are fully avoided. Meantime, one need only lay stress on the following points: (1) the coagulating solution must be carefully measured because of the subsequent effect which its slight acidity has upon the alkalinity of the copper solution: the rate of reduction of a cupric solution varies with its alkalinity; (2) the rate of reduction of the cupric solution depends also upon the rapidity with which the contents of the flask are raised to the boiling-point. Within limits, the more rapid the raising is, the greater the reduction in a given time; (3) the rapidity with which the contents of the flask are cooled—*rapid* cooling is necessary as the reduction proceeds well, at a temperature several degrees below boiling-point; (4) it is also of great importance that every solution which enters into the final mixture should be rendered air-free by recent

boiling, otherwise there may be a certain amount of reoxidisation of the cuprous salt by the oxygen in the solutions. If the method is carried out with reasonable care, and with the above precautions, we find that results are remarkably concordant. It should be mentioned that this method estimates all reducing substances in the blood under examination in terms of glucose, and in certain conditions this may have to be taken into account.

With regard to the normal sugar content of the blood, this may probably be taken as from 0·08 per cent. to 0·12 per cent., but after carbohydrate feeding there are occasionally considerable temporary fluctuations. Glucose does not escape normally by the kidneys until the threshold value of rather more than 0·17 per cent. and less than 0·18 per cent. is reached. In some cases the threshold may be lowered by various conditions, and in others it may be materially raised. It is thus obvious that one cannot assume that a patient who has suffered from glycosuria has become normal merely because of the disappearance of sugar from the urine, for this may occur whilst the blood sugar is still in considerable excess.

Numerous classifications of glycosuria have been proposed, and different forms of classification are useful in different types of investigation, but for general purposes Pollak's is probably as useful as any. He divides glycosurias into two groups; (*a*) those resulting from renal action; (*b*) those resulting from hyperglycemia, each of these main divisions being subsequently broken up into two or more subdivisions. Thus, in cases resulting from renal action he distinguishes (*a*) those without hyperglycemia and (*b*) those with hyperglycemia; phloridzin glycosuria being typical of the first group, whilst various renal poisons may induce the second type. In glycosuria resulting from hyperglycemia he distinguishes (*a*) those where it is independent of glycogen content of organs, as is found in true diabetes, and (*b*) where it is dependent upon glycogen content of organs and caused by sympathetic stimulation, which may be either central or peripheral. Central forms (analogous to piqûre) are due to drugs, such as caffein and strychnine, to asphyxia, and to stimulation of the sensory nerves. Peripheral forms may be caused by adrenalin. Allen has drawn up a much more elaborate table, which is useful in certain investigations, but is unnecessarily detailed for ordinary employment. It is based upon the division of glycosuria into "alimentary" on the one hand and "spontaneous" on the other. Any

"spontaneous" glycosuria may be regarded as due to some influence exerted upon one of four structures:—

Pancreas—Liver—Kidney—Nervous system.

Returning now to true diabetes to which our further remarks must be confined, it may be asserted with some confidence that the essential factor in its production is pancreatic insufficiency, and here Allen's work, following up that of v. Mering and Minkowski, has materially elucidated the findings of earlier experimenters, who had already noticed the constant association of operations on the pancreas with the production of glycosuria. The chief difficulties that have still to be encountered are largely due to the extremely inadequate knowledge of pathologists with regard to the details of pancreatic disease, as few glands of like importance have been less fruitfully studied.

Allen for general and clinical purposes groups cases into three classes; firstly, those where there is an extensive loss of parenchyma, involving islands and acini alike, and in the most extreme instances comparable to the Sandmeyer diabetes of dogs whose pancreas has been in large measure removed and where, as the remainder atrophies, a late diabetes supervenes; secondly, cases of selective injury of islands—such cases are practically never cured, and the destruction of the islands almost necessarily involves some damage to the acinar tissue; thirdly, cases in which the visible abnormality in both islands and acini seem too slight for a rational explanation of the diabetes. In view, however, of the wide divergence in toleration of ablation of large portions of the pancreas in different species of animals, more clinical and post-mortem observations are necessary. Probably the "margin of safety" in the human pancreas is narrower than in most animals.

Various causes have been suggested to account for pancreatic changes, and it is possible that in some cases the pancreas has been overstrained by carbohydrate excess or other dietetic causes. In other cases it is associated with pluriglandular disorders, the pancreas definitely suffering from an abnormal hormone stimulation. Constitutional or hereditary defects have little to support them. It seems probable that inflammation of the pancreas, whether due to infection or some other circumstance, is the likeliest cause of the vast majority of cases. In this respect one should perhaps note that Dr Ford Robertson's theory of a definite and characteristic organism being associated

with diabetes is not without some measure of support. In some of my researches in the wards of the Royal Infirmary, he kindly undertook to make cultures from the stools. These were not selected from diabetic patients only, but from patients suffering from other diseases who happened to be in the ward at the same time. Dr Robertson was able to separate from the great majority of the diabetic cases an anaerobic organism, which was never present in any of the other motions submitted, and which he considered to be the actual cause of the malady. The organism was difficult to grow, and therefore researches conducted in the wards did not yield conclusive results. I am, however, inclined to think that a connection exists between the organism and diabetes, but, of the two alternatives, either that (1) infection by the organism or its toxines induces the changes in the pancreas which reveal themselves as diabetes or, that (2) a disordered pancreas fails to secrete some constituent which, if present would inhibit the growth of this very delicate anaerobe, was left indeterminate, and in my own judgment the probability that its presence is the effect and not the cause of the pancreatic disorder appears the more probable hypothesis.

Assuming that pancreatic insufficiency is essential to the production of the disease, one can hardly over-emphasise the importance of correlation between laboratory and clinical workers in carrying out treatment. At every stage of treatment it is necessary that the clinical findings should be checked by somewhat elaborate tests in the chemical laboratory, and these tests can hardly be performed with sufficiently systematic and unbroken regularity by a clinician who cannot command the continuous time necessary for such work. The minimum amount of work required would seem to be (1) the occasional estimation of blood sugar, (2) the daily examination of the urine for sugar and other abnormal constituents, of which the most important are those belonging to the diacetic acid group. For all complications which threaten the diabetic patient, coma and its associated acidosis is the most dangerous and most often the cause of a fatal issue.

The subject of acidosis, which is in itself sufficient for a night's discussion, was dealt with very fully at a Meeting of the Association of American Physicians held in 1916. The following points that were there arrived at in summing up the theories of acidosis may be noted; the most essential

elements in the defensive mechanism are the mixtures of salts in the blood and body as a whole; of these the most important are phosphates and carbonates, the latter being associated with dissolved carbon dioxide. Such a mixture has a high degree of resistance to any change in its reaction; this resistance is known as its "buffer value." The carbon dioxide is the mobile factor in the combination, its physiological action enabling it to stimulate the respiratory centre whilst, as a consequence, its own partial pressure is controlled by the fluctuations in respiratory activity. There is a strict proportion between the various factors in the complex, and in some respects it is easier to measure the carbonates in the blood than the alveolar carbon dioxide which is difficult to estimate where the patient is unable to co-operate with the chemist. The larger the amount of alveolar carbon dioxide and total carbonates the less the degree of acidosis present in a given case. The production of acidosis may thus be shown to depend upon the rate of appearance of acid ions in the body and the rate of their elimination. It seems probable that in many diseases acidosis involves both factors; but there are further factors which to some extent differentiate the acidosis of diabetes from that in other diseases, and it has been suggested that this is due to the acids being associated with other by-products of toxic character. In diabetes itself there are two types of acidosis, in one of which air-hunger from stimulation of the respiratory centre is the main symptom, whilst in other cases the breathing is but little affected, and the patient sinks with symptoms of drowsiness and intoxication.

Various methods can be adopted for determining the degree of acidosis. On the one hand, the alveolar carbon dioxide tension may be estimated by some simple method, such as that of Fridericia, or the alkalinity of the blood may be investigated either by a direct method, such as that of Boycott and Chisholm or, with more elaboration, by Van Slyke's method which involves somewhat complicated laboratory apparatus. Various other procedures have also been adopted, such as that of Levy, Rowntree, and Marriott, for determination of the hydrogen-ion concentration of the blood by the indicator method, or Marriott's more recent process for investigation of the hydrogen-ion concentration after removal of the carbon dioxide, which appears to yield more accurate quantitative results. Miss Hawick and I have examined a number of

cases by the simpler procedure of Boycott and Chisholm, and we believe that for clinical purposes it is usually all that is necessary. Allen, after an elaborate discussion of these and other methods, considers that they are all open to some fallacies, and states that "if it comes to a question of the absolute minimum of laboratory work on which fasting can justifiably be conducted, the methods of choice are the Benedict qualitative sugar test for the urine and the Van Slyke determination of the bicarbonate reserve of the blood plasma, together with the nitroprusside reaction in the plasma."

With regard to treatment which has been most fully developed in the specialised hospitals of America, the latest monograph on the subject is to be found amongst those issued by the Rockefeller Institute for Medical Research *On the Total Dietary Regulations in the Treatment of Diabetes*, by Frederick Allen, Edgar Stillman, and Reginald Fitz. The main points which they have made are: that, in order to obtain satisfactory results, patients should be under hospital observation for at least a couple of months (1) to obviate the danger of acidosis during the initiation of the fasting method of treatment; (2) to govern with the greatest possible accuracy the individual diet; and (3) for the instruction of the patient, that he may carry out his diet after leaving hospital. The patients are seldom confined to bed, unless threatened by some complication or by severe acidosis. In order to spare caloric energy they are dressed warmly, as the low diet required for many cases leaves little energy to be utilised for warming the patient. The bowels usually require attention, but in many cases the dietary is so arranged that the use of active cathartics becomes unnecessary. This has been found to be specially the case where the patients are receiving bran biscuits during the days of fasting. Whilst in hospital a strict lookout is kept for alterations in respiration, pulse, and temperature, as these often give the earliest indication of some impending complication. Where the temperature, especially in children, falls below 96° F., it is a signal of danger and indicates that, even where the child does not seem seriously weaker, the under-nutrition of the fasting periods is leading to collapse, and the very strict limitation of diet must be relaxed.

Patients under treatment are weighed daily, but in estimating the value of the procedure it must be remembered that the weight may fluctuate considerably in consequence of the retention

of water during fasting, or, on the other hand, by its rapid excretion. Wherever rapid water loss occurs in patients who have a high D : N ratio there is a danger of a sudden onset of acidosis. On the other hand, water retention, even to the extent of marked œdema, is, in Joslin's opinion, one of the most favourable conditions when attempting to relieve a dangerons acidosis. In this connection it seems important, wherever acidosis is threatened, that the patient should be encouraged to take very large quantities of water, for in this way more of the toxic products appear to be eliminated.

During the fasting with which treatment is commenced, there is always a certain risk of the supervention of acidosis and, therefore, it is wise to insist that the daily intake of fluids should be approximately 2000 c.c. During the periods of fasting laboratory tests should be, if possible, carried out once or twice daily. The most important test which, one may note, is easy for the patient to be taught, is the qualitative one for urinary sugar. Whenever sugar disappears from the urine the spell of fasting may safely be terminated. Apart from laboratory facilities, acidosis can be estimated by the ferric chloride test in the urine, by the alkaline reaction of the urine and, especially, by noting the dosage of alkali which is required to turn the urine alkaline.

Quantitative tests should include nitrogen estimations; and the D : N ratio which, in carbohydrate-free diet, is a good test of the severity of the disease, should not be neglected. In severe cases the amino-acids in the blood and urine should also be tested. Many clinical observations have been made on the fat which appears in severe cases in the blood plasma, but little of scientific value has as yet resulted from these researches.

To avert acidosis, which is the chief source of risk in the fasting method, it is important to carry out Joslin's method, in which before the fast is instituted fat is entirely removed from the dietary, the protein is cut down by gradual degrees, and only when it has been eliminated from the diet an effort is made to institute the complete fast in which carbohydrates are also removed for several days. According to Joslin's experience, large doses of alkali are dangerous in acidosis. When the case is suitably handled in the earlier stages, the administration of alkali is unnecessary; when it is given as a last resort it not infrequently leads to the death of the patient, especially when it is given by the intravenous method. In many cases where

fasting is commenced acidosis is very much less severe in diabetic patients than in healthy subjects. When it does occur to a dangerous degree the urgency of the symptoms can generally be relieved by replacing a small proportion of the carbohydrates or, in some cases, where the D : N ratio is very high, by restoring a certain amount of protein to the diet.

When by fasting the patient's urine has become sugar-free the fast is abandoned, and careful efforts are made to reconstruct a dietary on which the patient can live without bringing back the overstrain on the pancreas. The construction of the diet need not offer any serious difficulty. What one aims at is to maintain the patient on a lower metabolic level than he had previously been living at, and to do so with such a combination of foods as to avoid the reappearance of sugar, Allen suggests the following very simple method of reconstructing a diabetic diet. The two basal principles are that the reconstructed diet should contain about one-sixth of the possible carbohydrate which he can tolerate without the appearance of sugar in the urine, together with 1·5 grams of protein, and as much fat as will enable him to have 30 calories, per kilogram of weight. The first step is to find out the amount of carbohydrate in the form of vegetables distributed over the various meals of the day, which, in all, would give the one-sixth of his maximum tolerance and, at the same time, to determine the caloric energy of that total. This having been done, the distribution of proteins over the day must next be considered, and it must be remembered that a certain amount of protein is contained in the vegetables which have already been given up to the carbohydrate limit decided upon. This amount must be subtracted from the total protein diet, the balance being made up of eggs, bacon, chicken, and cheese, or some such combination of foodstuffs. Having worked this out, one finds how many calories are still required by the patient in order to attain to 30 calories per kilogram daily ; the balance is then made up with various fats, such as butter, olive oil, bacon fat, or equivalent source of energy.

The only other complications, apart from acidosis, which have to be very carefully considered are those due to infections or to the necessity of surgical intervention. There can be no doubt that the risk of infection is much greater in a diabetic patient than in a healthy man, but the reason for this seems to be less dependent upon the presence of excessive sugar in the blood and tissues than upon the general lowered vitality of the

diabetic patient. On the other hand, surgical intervention, especially when accompanied by anæsthesia, must always remain a subject of great anxiety. Where general anæsthesia has to be used, it is probably best to employ gas and oxygen rather than chloroform or ether, which are particularly dangerous for patients whose liver is deficient in glycogen. Where local anæsthesia can be employed it is less hazardous. A surgeon who, in the light of present-day knowledge, apart from urgency operates on any patient without a previous examination of the urine for sugar, and who does not in any ordinary case submit the patient before operation to a thorough course of treatment for the diabetic condition, incurs a serious responsibility.

Opinion is divided as regards the place of drugs in the treatment of diabetes; but with increasing knowledge the use of drugs has taken a very subordinate place, and in the future, unless some drug can be discovered which will increase the pancreatic efficiency, it is unlikely that they will become re-established as a means of treatment. At the same time, the most that can be expected of dietetic treatment is arrest or retarded advance, but not cure of diabetes.

With regard to results and prognosis three factors offer themselves for consideration: (1) carbohydrate tolerance; (2) age; (3) clinical course of the malady when kept under observation. A case that, when it first comes under treatment, seems comparatively mild may prove itself both intractable and rapidly progressive; but, on the other hand, many cases which have every appearance of extreme severity are found to yield with surprising ease to the modern dietetic therapy. Whilst age offers no absolute guide, it is generally recognised that the danger of diabetes decreases as age advances. This is probably due, in part at least, to the much greater activity of metabolic processes in the young than in the old, as a consequence of which a pancreatic capacity which will prove quite inadequate to meet the calls imposed by growth and active body metabolism in the young may, nevertheless, meet any demand which is likely to be made on it during the later years when the vital processes are less vigorous.

Allen has considered statistically the results by decades, and he has tabulated in detail almost one hundred cases, mostly severe, with thirty-three deaths. The general conclusions seem to corroborate the view already expressed that the prognosis

depends largely upon the adequacy of the pancreas for the stress of life and that, whilst success has naturally been greatest with patients above the age of thirty, the outlook for younger patients has been greatly improved, and his experience supports his statement that, with properly applied treatment, cases of juvenile diabetes have been kept demonstrably free from downward progress for periods up to two years. It will be necessary, however, to carry on a larger series of observations for a much more protracted period before a final calculation can be reached. My own more limited experience has made me look much more hopefully on adolescent diabetes than I did ten years ago.

In the meantime, however, it may be regarded as satisfactorily established that the prospects of sufferers from diabetes of average severity can be enormously improved, and life can be rendered much more tolerable by the adoption of the modern dietetic rules, whose development and scientific working out in all important detail has been so largely due to the methods of co-operation between clinician and chemist that have been evolved in the richly endowed hospitals of the United States to an extent which is hardly realised in this country, although there are signs that here also the profession is gradually awaking to its responsibilities in that respect. It is also evident that there are some cases of glycosuria, apart from alimentary glycosuria, which are due not to irretrievable organic changes but to temporary disorders of the pancreas or of other endocrine glands, and obviously the glycosuria resulting from these is curable if the underlying temporary disorder can be rectified.

In conclusion, I wish it to be understood that the preceding remarks are in no sense an "exegesis" of the whole subject, but are intended rather to lead up to discussion by presenting a brief summary of the history, and of the clinical and laboratory findings, in diverse types of glycosuria.

The following points occur to me as possibly worth consideration in any discussion that may follow on this paper:—

(1) The condition of dextrose in the blood, whether free or combined and, if the latter, whether the pancreas supplies an amboceptor which enables the tissues to assimilate the sugar. On one hand, such a view is supported by certain workers, but, on the other, many chemists, especially those who are skilled in colloidal methods, decline to accept it.

(2) The nature of the influence of pancreatic internal secretion on the general metabolism of carbohydrate.
(3) The nature and prognosis of those cases where glycosuria occurs without any increase in blood sugar.
(4) The method of elimination of sugar by the kidney and the study of the "energetics" of the process.
(5) The suggested action of certain carbohydrate diets (*e.g.*, oatmeal), and whether these contain any substances which promote utilisation of sugar by the tissues.
(6) The question of treatment by under-nutrition in relation to pancreatic deficiency.
(7) The complication of pregnancy in the course of diabetes.
(8) The multiple origin of diabetes and its relation to general diseases such as gout and infective processes.
(9) The influence of age, employment, etc., on diabetes, and the possibility of short term insurances in view of the increased expectation of life in certain cases.
(10) The significance of special symptoms in reference to prognosis.
(11) The treatment of acidosis, especially with reference to the use of alkalies.

Discussion.

Dr Murray Lyon.—The remarks I would like to make on the subject of the prognosis of diabetes are based upon the examination of the records of about forty cases which have been under treatment during the past two years. At the present time the cases of diabetes must be divided into two classes with regard to the question of prognosis, namely, those who receive adequate treatment and those who do not, for the outlook of the diabetic subject has entirely changed since the introduction of modern methods of treatment.

Prognosis on Treated Cases.—Cure of diabetes, in the sense of removal of the symptoms and the cause of the disease, is very seldom possible, and since this is so, the ideal to be aimed at is to render and maintain the urine free from sugar and acetone, to remove other symptoms, and to allow the patient such a diet as will prevent him wasting and enable him to live a comfortable and useful life. Modern treatment renders this ideal attainable in the vast proportion of cases. The essential steps of treatment are as follows:—After the patient has been observed on ordinary diet for a few days, his food is gradually cut down to a fasting level, fats, proteins, and carbohydrates being

omitted in that order. Starvation is maintained until twenty-four hours after the urine has become sugar-free, and the diet is then slowly increased during the next three weeks. The rate of progress depends upon the response of the patient. In cases of treated diabetes, the future can be considered in two stages: (1) immediate results of treatment, and (2) the after history.

Immediate Prognosis.—The amount of improvement the patient will make while undergoing the course of treatment.

An estimate of the prognosis at this stage depends chiefly upon the severity of the disease and character of the response to treatment. In estimating the severity of the condition considerable help may be got from a number of methods of laboratory examinations. A rough indication of the severity is shown by the amount of urine passed in the day and by the percentage of the sugar present in the urine; but neither of these factors alone is satisfactory, for patients vary very greatly in the amount of concentration of the sugar that they are able to pass. A combination of these two factors giving the total amount of sugar wasted in the twenty-four hours is a better guide for all purposes. In this series of cases the loss of carbohydrate ranged from $2\frac{1}{2}$ grams to 400 grams in the twenty-four hours. While such an examination gives one an idea of the degree of the condition at the moment, it is of very little use in arriving at the prognosis, for some of these cases who excrete the greatest quantity of sugar eventually do much better than some of the apparently milder cases.

Examination of the Blood Sugar.—Investigation of the degree of hyperglycæmia can be made by examining the blood after the patient has fasted overnight. The height of this figure ought to indicate the degree of the deficiency in assimilating carbohydrate; but again, however, it affords no information as to the future prognosis of the case. Omitting a case of renal diabetes, the fasting levels of the sugar in untreated cases extend from 0.13 to 0.46. The arrangement of the cases according to this factor tallies closely with that under the urine examinations. It is to be noted, however, that the two tests are not quite parallel, for in many diabetics a high blood sugar may be present when no sugar is appearing in the urine (raised threshold). Under treatment the fasting level of the blood sugar rapidly diminishes and in many cases, after a few days fasting, reaches normal limits.

Blood Sugar Curves.—Another method of attempting to gauge the severity of the disease is by seeing how the patient reacts to a test meal of 100 grams glucose. Samples of blood are taken before the meal is given and at half-hour intervals afterwards during about three hours. The important points to notice in the examination of curves obtained in this fashion are the total height of the wave and the time at which it occurs. As a general rule it may be said that in new cases

the higher the fasting level of the blood the greater the maximum obtained—but the relationship is by no means strict. Many of the cases showed a maximum over 0.5 per cent. The apex of a curve usually occurs about ninety minutes after ingestion of the test meal. In the larger curves it is somewhat later. During these tests half-hourly specimens of urine are examined and all diabetics show a temporary increase in the amount of sugar wasted. The amount of sugar lost has been as great as 40 grams in some cases, while in others the loss is under 2 grams. None of these methods of examination gives more than the immediate condition of the patient.

A more reliable guide is to be got from observations of the patient's response to treatment.

Glucose test meals given before the patient leaves the hospital afford evidence of the benefit of treatment. The increased tolerance towards carbohydrate is shown by a reduction of about 25 to 40 per cent. in the height of the curve, while the amount of urine excreted during the test falls to a negligible amount (0 to 3 grams). In two striking cases, both men of about twenty-five years of age, the sugar wave, after taking 100 grams glucose, fell from 40 and 37 grams respectively to zero.

Examination of the urine will also give an idea of the improvement of the patient.

Freedom from Sugar.—With two exceptions all cases were made aglycosuric. One of the failures was a boy of fifteen who had a fulminating type of diabetes associated with severe acidosis. Attention was directed to combating this complication but the boy became homesick, was removed from hospital, and died shortly after. The other case had features which suggested that he was really a case of so-called "renal diabetes" (innocuous glycosuria). The time required to cause disappearance of the urinary sugar varied greatly (0 to 29 days), but the vast majority of the cases cleared up on the first or second fast day. In a few (three) the result was obtained on merely restricting the diet, omitting fat and protein, or halving the carbohydrate. The ease with which sugar is got rid of is no guide to the further progress of the condition, for some of these apparently mild cases have later given trouble by frequent reappearance of sugar during the earlier stages of dieting. On the whole the more severe cases required longer to become sugar-free. Where the fasting was unduly prolonged a break was made each fourth day and some food was given. Further experience of the disease, and especially the fact that most severe cases usually clear up about the fourth day, has suggested that other factors are at work in these refractory cases. These are chiefly nervous influences and toxæmias.

Re-appearance of Glycosuria.—A trace of sugar, occasionally

more, commonly occurs during the stage of tolerance estimation usually between the twelfth and sixteenth days. Return of sugar is met by the imposition of an extra fast day and this nearly always proves effective. Little weight should be attached to such an occurrence, it simply means that the dietary ladder should be mounted more slowly. When the sugar returns on the first or second day of dieting the condition is more significant and troublesome.

Frequent reappearance of glycosuria, like its persistence after fasting, demands further investigation of the patient. The influence of the nervous system on the carbohydrate metabolism may be profound. The commonest sources of trouble in this direction are worry, anxiety, and excitement. Recognition and removal of the cause produce immediate effects.

Examples.—Worry about home affairs—three days' sugar; wage-earner's anxiety about his future—frequent return of glycosuria; excitement of football match—sugar in next sample of urine.

The influence of toxæmia is also of great importance. There can be no doubt that sepsis is harmful to the carbohydrate assimilating mechanism, aggravating the existing difficulty. It is interesting to note that the diabetic is believed to be specially susceptible to infections. In the absence of more obvious causes, local foci of infection should be looked for. The commonest source of suppuration in diabetics is pyorrhœa alveolaris, and attention to the teeth in a case which has resisted repeated fasts over a period of twenty-five days resulted in sugar freedom four days later.

Other Examples.—Gangrene of toes—may retard sugar freedom but tends to heal up when sugar free; boils; rheumatic fever; gallstones—question of pain.

Ketonuria.—The presence of ketone bodies in the urine is of little help in estimating the severity of the disease in giving a prognosis. They may be present in mild cases and absent in severe ones, and it should be remembered that ketonuria may be quite easily induced in healthy individuals by simply starving.

The excretion of these bodies shows that fats are being imperfectly broken up in the system, and that insufficient carbohydrate is being taken to preserve the balance between the foodstuffs. The urine should be carefully examined for acetone and diacetic acid. A small quantity is of little account but large amounts spell danger from acidosis and coma.

Ketonuria of varying degree was present in about half the cases in this series on first examination. It usually persists for a very much longer time than the glycosuria, a point that is of some interest to examiners for life insurance. Three to thirty-six days were required after commencement of treatment before the tests became negative.

In one case acetone disappeared from the urine the day that fats were omitted from the diet. The patient was an extremely emaciated youth, so much so that practically no fat remained (aged 19, 5 st. 3 lb.).

In several cases ketone bodies were absent from the urine when first examined but appeared as soon as the carbohydrates were omitted from the diet, and the reactions continued positive until sufficient carbohydrate was added to the diet to restore the balance.

The prolonged occurrence of acetone and diacetic acid in the urine delay progress, since fats cannot be used in large quantities to build up the calories of the diet to a satisfactory level.

Diets attained during Treatment.—Those patients who remained only for a very short time in hospital reached a diet of about 1600 calories, but the majority of the cases were consuming well over 2000 calories before discharge. At first the bulk of the carbohydrate is in the form of green vegetables, tomatoes, then oatcakes and porridge are cautiously added, and many of the cases have tried a small quantity of ordinary bread before they left. The amount of protein is just short of that of ordinary diet, while the consumption of fats depends upon the absence of ketone bodies in the urine, and on the quantity of carbohydrate consumed.

Body-Weight while in Hospital.—All patients before treatment complained of having lost weight to a greater or less degree. During the earlier stages of treatment the further wasting takes place, from a few pounds to a stone being lost, but before leaving hospital the patient is rapidly making up again.

Prognosis for the Period of Maintenance.—The after history of the case depends to a great extent on the intelligence and reliability of the patient. Before discharge from hospital the patient has his disease explained to him, he is told the significance and the danger of glycosuria and how to avoid it. He is told in a general way what foods he can take, and how much of them, and how to know when he is exceeding the limit. To this end he is advised to weigh himself regularly each week; loss of weight implies glycosuria. The patient is taught how to examine his urine for the presence of sugar (Fehling's method), and is told to examine a mixed sample of urine daily. The carbohydrate tolerance may continue to improve after the patient leaves hospital, but the patient is warned against continuously adding to the quantity of carbohydrate he is taking. It is better to continue to take a sparing diet which will keep him below normal weight, than to have sugar constantly reappearing in the urine.

The diet that can be eventually consumed varies greatly. Some

cases continue to struggle along on little more than they were taking while in hospital, while others, even the apparently severe cases can handle ordinary diet and bread with impunity. In either case the physical well-being of the patients is better than when treatment was begun, and they remain quite free from the old distressing symptoms.

Many of the patients are able to return to their ordinary occupation and can do even hard work without trouble. Others find (on poorer diets) that they become easily fatigued and have to take on lighter duties.

The resistance to intercurrent disease must depend on the condition of the body at the time. The risk of infection must be avoided by those on low diets, but the dangers are probably less than in untreated cases.

The information available is not sufficient to make any dogmatic statement as to the expectation of life, but it is believed that with due care many diabetics ought to live as long as other members of the community.

Dr Fowler congratulated Dr Rainy on the admirable summary with which he had opened the discussion. He had been interested to find that Dr Murray Lyon, with every opportunity of applying the various tests, and a much larger experience of the disease than he (the speaker) had had, found it difficult to give a prognosis in diabetes. This, after all, was perhaps not surprising, because in glycosuria we are only dealing with a symptom, and are ignorant of the nature of the underlying lesion. It might be assumed that in some cases of diabetes the disturbance was a purely functional one, while in others there was a progressive organic disease of the pancreas, and we had no means of distinguishing between the two. To illustrate the difficulty he had, he referred first to the very remarkable case shown by Dr Lyon at the Society about a year ago—of a young man, with very high blood sugar and very low carbohydrate tolerance and much disturbance of the fat metabolism—a case which appeared to be a very unfavourable one, but in which what almost amounted to cure had occurred. At the other extreme, he took the case of an elderly lady, whose glycosuria disappeared from the urine very quickly under starvation, and who left hospital with a carbohydrate tolerance of 50 grams, on a good diet well within her tolerance. This was apparently a mild case, and yet her tolerance rapidly diminished, and she went from bad to worse and died of coma about four months later. Again, he had had two patients in hospital at the same time some two years ago; one was a man of forty, whose sugar quickly disappeared from the urine, and who went home on a fairly good diet containing about 20 grams of carbohydrate. He had no acetone bodies in the urine while in hospital; he kept

absolutely free from sugar for about eighteen months, and then it suddenly reappeared and he died in coma. This was a case which seemed favourable, as the man was intelligent and in a position to diet himself properly, and yet the patient had not lived so long as the other case, a working lad of twenty, who had been several times in hospital, whose blood sugar was high, and whose carbohydrate tolerance was very low. His urine always containing acetone, four days of starvation was required to make it sugar-free, and sugar returned whenever the amount of carbohydrate in the diet rose above 4 grams. Repeated attempts to raise his tolerance had failed, and he had had practically all the time both glycosuria and ketonuria. Yet he was still alive and suffering little from the disease. The speaker thought, therefore, that it was almost impossible to predict how a case would turn out, apart from watching its course under treatment. He made the suggestion that some information might be got by attempting to estimate the power of the patient to deal with fats: when once the diet was stabilised a measured quantity of fat might be added, and its effect measured by the estimation of the ammonia nitrogen in the urine.

He also referred to the problem of so-called renal diabetes, two cases of which had been under his observation for ten and eighteen years respectively. Both these patients had been turned down for life insurance, in both of them every time the urine had been examined it contained about 1 per cent. of sugar, while the blood sugar was low —about 0.07. Both of these men were perfectly well and led active lives, and had never had a symptom of diabetes. It was only within the last few years that we had been able to recognise cases of renal diabetes, and sufficient time had not yet gone by to make one quite sure that the condition was harmless. In one of the two patients referred to, for example, there was said to be a strong family tendency to diabetes. He would therefore be very glad to hear if any member of the Society could remember having met with a case in which glycosuria had persisted for many years without producing any symptoms whatever, and then had developed into true diabetes.

Dr Somerville emphasised the intelligent co-operation of the patient as the chief essential in the treatment of diabetes in private practice. A recent case of his, with a super-intelligent son-in-law who tested the urine each time it was passed (seven or eight times a day), showed that on reduced ordinary diet without sugar, Benedict's test was positive only twice or thrice a day. The most usual time for the urine to be positive was after supper. The patient was taking regular walking exercise three to six miles a day. A mixed twenty-four hours' specimen in this case would, he thought, have been negative on several days. Dr Haldane stated recently in Edinburgh that the first clinical symptom of acidosis from experimental ingestion of ammonium chloride was

breathlessness on exertion, so Dr Somerville suggested that in treating patients who were taking regular outdoor exercise we need not fear acidosis as long as they were free from shortness of breath.

Dr F. Porter raised the question as to when the condition of glycosuria could be regarded as having passed into diabetes. It was known that glycosuria could disappear without special dietary treatment, as in one of his patients with numerous boils and glycosuria, in whom the cure of the boils by the use of yeast was followed by the disappearance of the glycosuria.

Dr W. S. M'Laren told of a stout, middle-aged woman to whom he gave 5 grains daily of thyroid extract for six weeks. Glycosuria then developed, and the case ended fatally in coma four months later. In this case there was a hereditary history of diabetes and an antecedent history of gall-stones ten years before.

Dr Goodall said he thought that too much stress might be laid on the caloric value of the diet. This was especially the case in children in whom the requirements for growth were not easy to assess. The biological value of proteins varied although their caloric value might be identical. Thus a diet of wheat was of much greater value than a diet of peas, although their caloric value might be the same. He recognised the value of the various laboratory tests, but in the ordinary run of cases he was content to reduce the diet until the urine was sugar-free, and then to add carbohydrate in the form of bread in quarter ounces until the limit of tolerance was reached. Thereafter the effort of some equivalent carbohydrates might be tried. There were patients who could not be kept free of glycosuria, but a certain restriction of dietary would keep the sugar loss at a low level and any increase in the diet led to a sudden jump in the sugar wastage.

The President said he was glad to hear the tribute paid to the work of Dr Guelpa of Paris. He himself had been instrumental in bringing Guelpa to London in 1910 to address the British Medical Association, but his views at that time received little attention.

Dr Rainy in reply agreed as to the importance of seeking out any source of infection and dealing with it. In regard to diabetes in young children, some of these were of nervous origin, and in these the prognosis was good: they corresponded to the adult cases of temporary glycosuria after nervous strain. A normal level of blood sugar with glycosuria was another benign type of case. With regard to the distinction between glycosuria and diabetes, it was a safe rule to call the former diabetes until it was proved not to be so.

THE PROGNOSIS OF CROUPOUS PNEUMONIA IN THE OLDER PATIENT, WITH A SUGGESTION AS TO A RADICAL MODIFICATION OF THE USUAL PLAN OF TREATMENT.*

By ROBERT A. FLEMING, M.D., F.R.C.P.E.

It is generally recognised that croupous pneumonia increases in risk after full adult life is past, and that after the age of forty each decade means a steadily increasing death-rate, until in old age the mortality becomes extremely high.

Further, it is common knowledge that any cardiac lesion, such as endocarditis and pericarditis, and a number of heart affections associated with, or resulting in, dilatation, gravely increase the patient's risks. There are also many other conditions to which it is almost superfluous to refer and most of which prove fatal, such as alcoholism; so-called terminal pneumonias—complicating diabetes mellitus, cancer, Bright's disease and so forth; and cases in which pneumococcal toxæmia develops.

The chief risk which a strong adult runs is undoubtedly the development of a double pneumonia, or to put the matter in another way, the steady involvement of more and more of one lung and later the spread of the disease to the other. In the older patient there appear to me to be two conditions which render the prognosis peculiarly grave, and it is with reference to these and to a possible means of prevention that I wish specially to deal in this short paper.

A pneumonia case gives rise to anxiety when the unaffected lung becomes œdematous, and when further a definite and spreading pleurisy becomes evident over that lung. In many cases I have found that the advent of pleuritic friction over the unconsolidated lung indicated the speedy death of the patient and appeared to be a direct sequel to the œdema.

One knows that any enfeebled individual, if confined to bed, and specially if he has to lie flat, rapidly develops œdema of the lungs; and it is little wonder that in a patient with pneumonia the overstrained right heart should dilate and so probably directly cause the onset of the œdema, the degree of œdema having a direct relationship to the amount of dilatation of the

* Read 15th February 1922.

right heart present. Probably the drop in vaso-motor tone so often present in pneumonia is also a factor in producing œdema.

In 1913 I wrote a paper on ante-mortem clotting of blood in fatal cases of croupous pneumonia. Since making these observations I have invariably examined the jugular veins to see if there was any evidence of undue engorgement, and have also listened with special care to the second sound in the pulmonary area. Its enfeeblement suggests not merely a dilated right ventricle exceeding its limits of compensation, but also the possibility of blood clot mechanically obstructing the closure of the cusps. I do not desire again to discuss the arguments brought before the Society at that time, but would merely suggest that it is possible that such clot where it occurs may be an important factor in increasing the œdema in the air vesicles. The pleurisy is certainly of infective origin, is directly due in most cases to the pneumococcus and is secondary to the œdema.

In numbers of older patients with croupous pneumonia I have watched the gradual increase of the disease, and these two signs of grave portent, œdema and pleurisy, appear in the lung previously uninvolved. My contention is that an œdematous lung is below par, and readily becomes attacked by the pneumococcus or by other organisms, and that the œdema is the early stage of involvement of the unaffected lung and is followed by the pleurisy.

I have consulted a large number of authoritative works on croupous pneumonia and its treatment, and the universal opinion, as regards part of the treatment, is the same as that which I was taught myself. Rest is enjoined with the special object of conserving the heart, while most authorities urge measures for the relief of the spasmodic cough by sedatives and specially the use of opium. It is almost superfluous to add that cardiac tonics are recommended by everyone.

We all know that if a pneumonia patient eats and sleeps well he will get well, but sleep obtained by complete respite from coughing may be bought at too high a price.

Some time ago I had an experience which revolutionised my own ideas with regard to the value, or I should rather say the danger, of sedatives and of adhering too closely to the principle of absolute rest. The patient was aged about fifty. The heart, although there was no actual valvular lesion, showed

a definite and increasing degree of dilatation as the pneumonia developed. On the fifth day I found the heart intermitting every fifth beat, the presence of marked œdema and definite friction over the left base, while the original pneumonic consolidation had been limited to the right lower lobe. That afternoon when visiting the patient I was alarmed to see him sitting bolt upright in bed coughing violently and holding on to his two attendants. The spasmodic cough lasted for several minutes and after the attack I found to my surprise that the intermittent heart had become regular, and when I again saw him some hours later, several attacks of coughing having occurred in the interval, the friction had disappeared and the œdema was much diminished.

Uninterrupted recovery followed, but no attempt was made to restrain the spasms of coughing except by giving remedies to render the sputum less viscid, while I trusted to poulticing for the relief of pain and gave no medicinal sedatives whatsoever.

It is a remarkable fact that a dry pleurisy at all events can be made to disappear by deep breathing, and I can recall a case of dry pleurisy of tuberculous nature which I recently showed to my clinique at the Royal Infirmary. The friction was palpable and I asked my students to come and feel it. A dozen came down and went away in a few minutes satisfied, and then I found that the thirteenth man failed to feel anything. I suggested that they might listen with the stethoscope to the friction if they could not feel it, and again a party of about twelve students quickly heard the definite pleuritic friction, but once again there was a stoppage. I found that the friction at first easily palpable had absolutely disappeared after a sufficient number of deep breaths had been taken by the patient, so as to get over the thirty odd students who examined him. It may be asking too much to suggest that extensive and acute pneumococcal friction could disappear by deep breathing, and it is more probable that the freeing of the unconsolidated lung from the œdema permitted of the rapid arrest of the pleurisy in the pneumonia case to which I referred a few moments ago.

I can recall cases where, if the spasmodic cough had been encouraged and not soothed, I firmly believe the result in certain of these cases would have been very different from what it was. If I might say so, we have been too much afraid of heart failure and have insisted too much on rest in the recumbent posture. Might I also suggest that in broncho-

pneumonia in older patients a similar plan might be adopted, much as one does in the case of very young children suffering from that disease, risking the failing heart by raising the patient and so obviating the detrimental effects of gravity. Many of us already adopt this procedure in broncho-pneumonia, though it is held to be unorthodox in cases of croupous pneumonia. I think that at this time of the year and with so much influenzal pneumonia in our midst, anything that one has personally found of marked benefit ought to be submitted at least for the criticism and consideration of one's brother practitioners.

Discussion.

Dr Whitridge Davies said that disease was now being more studied from the point of view of function, but this method was still somewhat neglected in respiratory disease. In croupous pneumonia there was a deficiency of oxygen in the arterial blood in direct proportion to the amount of cyanosis, and cerebral symptoms appeared when the arterial oxygen was below 80 per cent. Anoxæmia was the important factor in lobar pneumonia, and was the leading indication for treatment.

Dr J. D. Comrie corroborated Dr Fleming's remarks from his own observation and experience. In one old lady of seventy-five, with extensive pleurisy and bronchitis, and in a dangerous condition, he stopped sedatives, encouraged coughing, and had the patient propped up in bed. The patient recovered.

The President said he was surprised to hear that the use of opium was still advised by modern authorities; his own view was that in pneumonia it was a poison. Recent experience, including that of the South African War, had proved the benefit of open-air treatment in acute pneumonia; and the beneficial action was no doubt due to the stimulation of the respiratory activity. It was his practice in suitable cases to promote this respiratory activity by a kind of artificial respiration carried out by relays of assistants and nurses.

Dr Fleming replied that he was well aware of the value of oxygen and used it freely. As to opium, quite a number of modern authorities advised its use. The suggestion of artificial respiration was a good one. He wished to draw attention to the spasmodic cough in pneumonia: its action was beneficial and should not be discouraged.

DEMONSTRATION OF PATIENTS WEARING ARTIFICIAL LIMBS FOR AMPUTATIONS AT DIFFERENT LEVELS IN THE LOWER EXTREMITY.*

With an Explanation and Demonstration of the Type of Artificial Limb used in each Case.

By CHARLES W. CATHCART, F.R.C.S.

Chopart's Amputation.—In this instance the patient who was to have come had recently died. The appliance he had used with complete satisfaction for the last two years was shown. From suggestions given to him it was worked out by Mr Greenslade, manager of the Rowley firm, for this man, and has been used with equal success for other cases. It consists of a leather anklet and wooden sole-piece (fitting the stump), to which is hinged a toe-piece representing the amputated portion of the foot. It has no steels, gives full play to the ankle, and is worn with an ordinary pair of boots. It costs £5, seldom needs repair, and weighs about 1 lb. This appliance is not on the Consolidated Government list but has been granted for several cases by special request. The standard appliance has strong side steels, permits of only slight ankle movement, and being on this account subject to great strain, frequently breaks down. It weighs $3\frac{1}{2}$ lb. and costs £10 to £12, apart from the price of a special boot which is required, and which costs about £2, 5s.

Syme's Amputation.—The patient D. was seen to walk without an appreciable limp. The appliance he wears is of a pattern recently improved. The weight-bearing pad is above, not, as formerly, below the artificial ankle-joint. This avoids friction on the face of the stump. The steels are now arranged to bear the great strain upon them much better than before, and they last longer. Formerly a specially made boot was necessary, now an ordinary pair of boots is sufficient.

The appreciation of Syme's stump has, if anything, been enhanced by experience in the recent war, although it is not to be preferred to a Chopart's stump, where the conditions necessary for the success of a "Chopart" are present.

The only modification that seems worth considering is that of dividing the bones at a slightly higher level than before, so as to make the stump a little narrower.

* Given 1st March 1922.

Amputations in the Lower Third of the Tibia.—Reference was made to this level of amputation only to condemn it.

A patient was shown on crutches, having had to have a re-amputation recently, because his former stump, a little above the ankle, had proved so unsatisfactory for use with an artificial limb.

Amputations in the Middle Third of the Leg and up to within 4 in. of the Knee-joint.—One or two cases were shown with excellent results in the use of artificial limbs.

Stumps 2 or 2½ in. below the Knee-joint.—This level was advocated as giving a most useful thigh-stump with its bearing on the bent knee. A patient, W. G., was shown walking with confidence and ease and able for a long day's hard work on the artificial leg.

The socket for the stump is of leather which is laced up after the stump has been introduced. A stump longer than 3 in. at most projects unduly backwards, while one of about 2 in. is not noticeable through the trousers.

Disarticulation at the Knee-joint.—This also was recommended as giving an excellent stump for use with an artificial limb, nearly as good as the bent knee-stump, the artificial limb required being very similar. The broad rounded articular surfaces are covered by skin which although thin is accustomed to bear pressure. Hence end-bearing has been found very satisfactory.

C. K. was shown wearing this type of leg. He is a plumber and works with his father. He climbs ladders, works on roofs, and is able to do practically all the work of his trade. He is thoroughly satisfied with the stump.

Amputations through the Condyles—*i.e.*, Gritti-Stokes', Carden's, Spence's, etc.—(1) Several *Gritti-Stokes'* amputation stumps have been seen at Edenhall, but end-bearing of the stump has been the exception.

When end-bearing is present the stump is excellent for an artificial limb, the construction of which is similar to that for disarticulation at the knee. When, however, full end-bearing is not possible, the artificial limb causes great discomfort, and is very difficult to adjust.

(2) *Above the level of a "Gritti-Stokes,"* should it be approved, the next best site is that in the middle third of the

femur, in the distal portion if possible. This excludes certain other frequently used amputations through the condyles or just above them. These are practically never end-bearing, and they do not leave sufficient space for a satisfactory knee-joint. The few additional inches of femur lost by going higher, while not valuable for leverage, give room for a satisfactory artificial knee-joint with knee control.

Two patients with Gritti-Stokes' amputations were shown.

One, J. F., had an end-bearing stump, and was quite satisfied with it and the artificial limb with which he has been fitted.

The other, A. F. B., has a stump that cannot bear pressure on the end although without any apparent reason. He has been unable to use the typical leather bucket, and now wears a wooden bucket, taking the weight at the tuber ischii. The result, however, is not so good as it would have been had his stump been 3 or 4 in. shorter. The minimum space above the knee required for a "knee-control" joint (now the standard pattern) is 3 in. from the line of the joint.

Amputations in the Middle Third of the Femur.—These constitute typical thigh-stumps, and are supplied with a wooden bucket, taking the weight on the tuber ischii.

At the knee an ingenious device enables the wearer to straighten the leg by means of cords which pass over his shoulders; thus by an imperceptible raising of his shoulders he can straighten his knee should he stumble and also regulate his pace as desired. When any form of spring is used to straighten the leg the speed of the artificial leg action is uniform, whatever be the rate of action of the sound limb.

J. J. was shown walking actively with a mid-thigh stump fitted with the knee-control.

Short Thigh-Stump—Say $4\frac{1}{2}$ in. to 5 in. from the perineum or about 7 in. from tip of great trochanter. In fitting this stump difficulties are met with from the tendency of the stump to be flexed and abducted owing to the loss of part of the extensor and adductor groups of muscle. During the healing of such stumps care has to be taken to minimise these faults of posture. A pelvic band in such cases is fixed with a joint to the upper and outer part of the bucket to compensate for loss of adductor power and for the imperfect grasp of the bucket on the short stump.

Case of W. shown. This man is an artificial limb maker, and is on his feet all day.

Amputations within 2 or 3 in. of the Hip-joint and Disarticulations at the Hip.—These cases require a bucket for the whole half of the pelvis known as "a tilting table." Below this are parts similar to those for thigh amputations with the necessary modifications of the upper part of the thigh piece to admit of sitting.

Tilting Table for Disarticulation at Hip.—A. B. was shown wearing this type of leg. His walk is slow but much better than what would be expected, and he can sit down easily by releasing a catch which allows of flexion at the hip.

Tilting Table with Peg Leg.—E. A. M. was shown wearing this limb. He prefers a peg leg as being lighter for his work. He has a green-grocer's shop, and lifts heavy bags of vegetables without difficulty.

Beaufort Legs.—Mr Cathcart showed two civil patients recently supplied with this type of artificial leg, for stumps above and below the knee respectively. These limbs were invented by the late Count Beaufort, and have been used in Rome, Paris, and London, although in the two latter cities they have gradually fallen out of use. They consist of a light beechwood frame-work, and are used with a stiff knee in walking for thigh cases. The foot has a curved sole and no ankle movement. In thigh cases the weight is borne on the tuber ischii on a half metal ring uniting the two wooden uprights. In below-knee cases the weight is borne partly below the knee and partly on the thigh. They are very strong, and yet are lighter than any mechanical leg. In price they are less than a third of the price of mechanical legs, while they are much less expensive in upkeep.

When these limbs are worn the framework is concealed by the clothing, and the foot has nearly as good an appearance as that of any of the more expensive artificial legs.

Discussion.

Mr Caird congratulated Mr Cathcart on the successful issue of his long-continued advocacy of the Beaufort limb. He naturally agreed with Mr Cathcart's conclusions, and thought it interesting that they had no examples of osteoplastic operation below the knee represented in the most admirable demonstration they had witnessed.

Sir David Wallace thanked Mr Cathcart for his most interesting demonstration, and remarked that he thought all would agree with him in saying that Mr Cathcart was the best selection that could have been made for the work, the results of which he had shown that evening. No one was more interested in the subject of artificial limbs, and from the surgical as well as the mechanical side he was particularly well qualified to carry out the work. He referred to the important place that amputation had taken in the surgery of the war, and thought that the demonstration which they had just witnessed showed the acme of success which had been attained in supplying suitable artificial limbs. There were three points which he thought of importance:— (1) the stump after amputation; (2) the benefit derived by the use of provisional limbs; (3) the best form of artificial limb for practical purposes. There was no doubt that to sacrifice length to obtain a good stump was imperative—a stump which could bear pressure, if possible, and one which at least enabled the limb maker to supply a satisfactory artificial limb.

The Beaufort limb was an excellent limb, and he was glad that Mr Cathcart advocated its merits. It was light, strong, and cheap, and probably served the purposes of the working man better than more elaborate limbs. Personally, he believed that in many cases for every-day work the peg leg was better adapted than any other for the working man.

Mr Cathcart in reply said that provisional limbs would be of advantage in civil practice as they had been in military practice. They reduce the size of relatively recent stumps, and thus obviate the need for early renewal of the bucket of the permanent artificial limb. He considered that the "plaster pylon" was more efficient than the "fibre cone" type, as it fitted the stump more accurately, and therefore exerted more uniform pressure.

With regard to permanent peg legs, the men were allowed to decide whether or not a peg leg was to be one of the two artificial limbs granted them by Government. Fewer were asked for than had been expected, apparently for several reasons. Thus a peg leg is unsuitable if the ground is soft, or has a slippery surface; if gratings or narrow apertures are met with in the men's work. Again, many men wished to avoid the appearance of being disabled for various reasons.

INTERNAL STRANGULATION OF THE SMALL INTESTINE CAUSED BY BANDS, ADHESIONS, AND KINKS.

By FRANCIS M. CAIRD.

THE general symptoms of internal strangulation, whether caused by bands, adhesions, or associated kinks, are similar to those which characterise ordinary strangulated hernia. External manifestations at the local sites are, of course, lacking, nor does the relatively thick abdominal wall permit of the free palpation and examination afforded through the thin coverings of an external hernia. The very absence of any external protrusion or local tenderness should thus all the more concentrate attention upon the gravity of the conditions as evidenced by the sudden onset of severe colic and vomiting. In addition to epigastric pain and nausea the bowels refuse to act although the last motion prior to and sometimes just preceding the attack is usually normal. The condition is all the more serious since pathological changes of the greatest moment are progressing rapidly within the peritoneum from the very onset. These changes differ in an important respect from what occurs in strangulated hernia, since they are not in the first instance confined within an outlying serous sac more or less shut off by inflammatory reaction from the general peritoneal cavity. Hence their gravity—the fear of an impending general peritonitis. Unfortunately it happens that only too often is the diagnosis and consequent treatment delayed until surgical aid becomes a forlorn hope. The crying urgency of the case calls for rapid investigation, and however much the slip-shod diagnosis of "acute abdomen" may be deprecated it at least arouses the practitioner to recognise his responsibilities. Nor is an exact diagnosis requisite, for surgical exploration will speedily make it precise. However, if a history can be elicited which recalls antecedent attacks of hernia, peritonitis, appendicitis, typhoid fever, tubercle, ovarian troubles or the like, it may aid in forming an opinion. Such ailments favour the possibility of visceral and omental adhesions: when no other previous or recognisable cause can be established, the presence of internal strangulation due to a band or to one of the rarer forms of internal hernia is suggested.

Internal Strangulation of Small Intestine

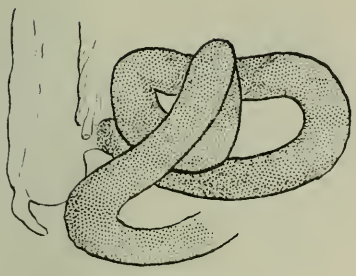


FIG. 1.—Case II.

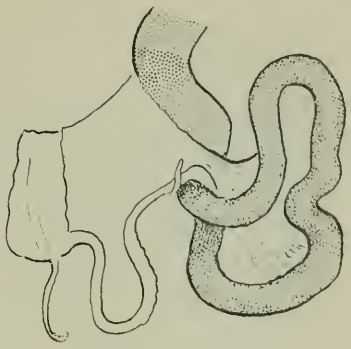


FIG. 2.—Case III.

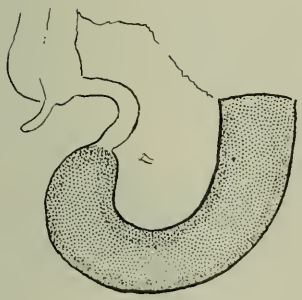


FIG. 3.—Case IV.

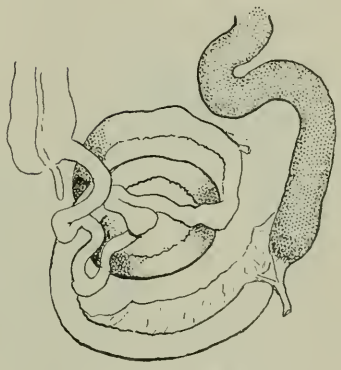


FIG. 4.—Case V.

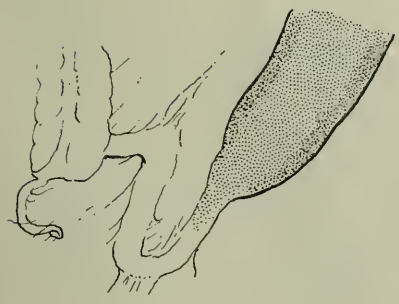


FIG. 5.—Case X.

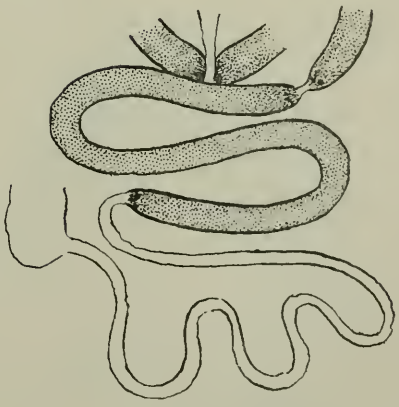


FIG. 6.—Case XI.

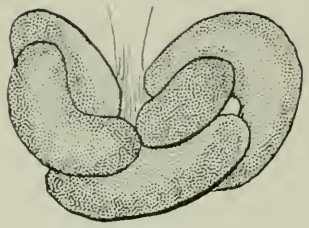


FIG. 7.—Case XIX.

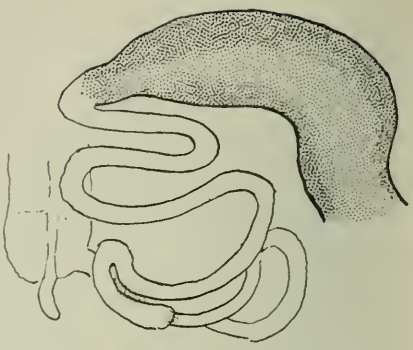


FIG. 8.—Case XX.

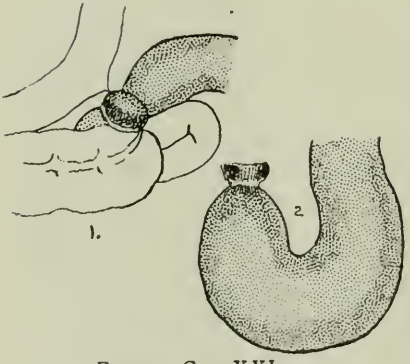


FIG. 9.—Case XXI.

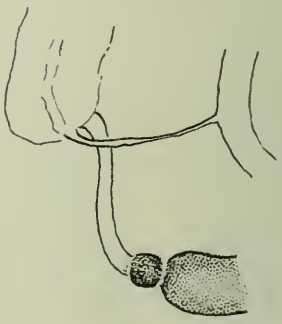


FIG. 10.—Case XXI.

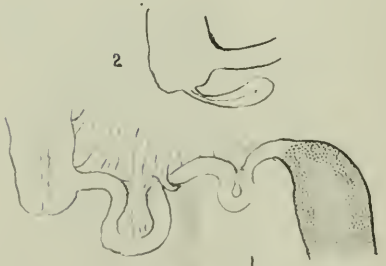


FIG. 11.—Case XXII.

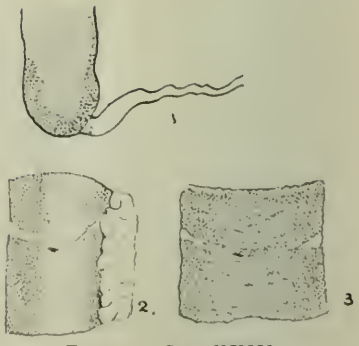


FIG. 12.—Case XXIII.

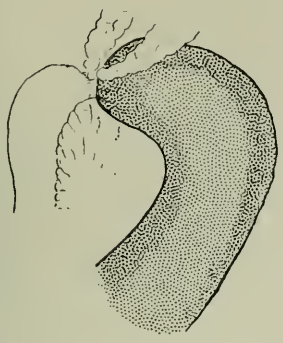


FIG. 13.—Case IX.

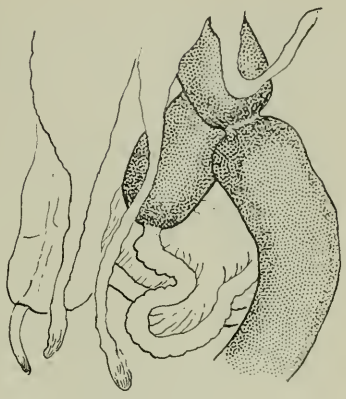


FIG. 14.—Case XII.

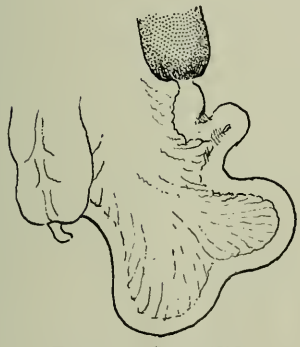


FIG. 15.—Case XIV.

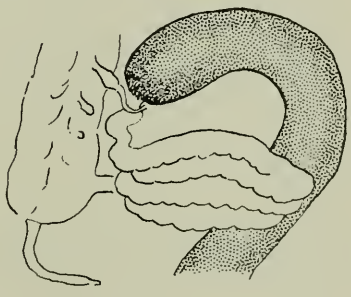


FIG. 16.—Case XV.

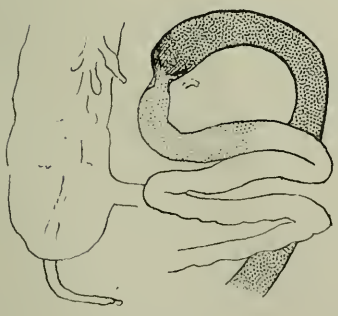


FIG. 17 —Case XV.

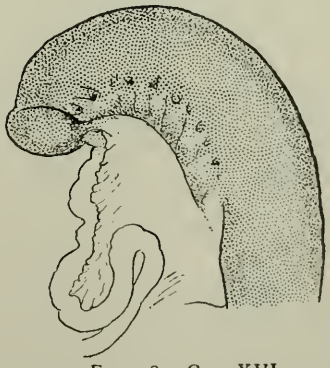


FIG. 18.—Case XVI.

Internal Strangulation of Small Intestine

The following 23 consecutive cases submitted to operation in hospital during the last twenty years revealed conditions which may be roughly classified under four causal heads: Bands, Types I. and II.; Omental Tags, Type III.; Adhesions. Type IV.

I. *Type of Strangulated Hernia.*—Of this there were two cases. In Case XXI. (Fig. 9) there was found a fibrous cord extending from the apex of the appendix to the anti-mesenteric border of an adjacent coil of ileum which had completely encircled and strangled a small portion of bowel. On freeing this cord and liberating the bowel (Fig. 10) inspection of the parts concerned showed the customary sequence of changes met in strangulated hernia: namely, the distended entrant gut, actively congested; then the first anæmic zone of constriction; next the strangled segment, passively congested; then the second anæmic compression zone, followed in its turn by the pale, empty, contracted bowel beyond.

The second case (VI.) disclosed a knuckle of bowel strangulated by a thin band, the extremities of which arose closely together from the iliac mesentery and then formed a noose. Such types appear to be rare within the abdomen, but are well represented in examples of internal hernia into pericæcal fossæ, etc.

II. *Type with Solitary Constriction only.*—The proximal bowel is greatly distended and congested, terminates at the anæmic ring of constriction, and is succeeded by the distal pale empty gut. Of this type there were seven examples. Cases II. (Fig. 1) and IV. (Fig. 3); Cases IX. (Fig. 13), XIV. (Fig. 15), XV. (Figs. 16 and 17), XVI. (Fig. 18), and XXIII. In Cases IX., XIV., and XXIII. the constricting cause was not discovered; in the others, at least one root of the band will be seen figured.

III. *Type with Multiple Constrictions.*—The proximal bowel as usual greatly distended; that intervening between the constrictions moderately so and congested; the terminal coil of course empty. In this series long omental tags seem to play a great part, and were undoubtedly the active agents in Case XI. (Fig. 6) and Case XII. (Fig. 14).

IV. Type with Multiple Constrictions mainly due to Adhesions complicated with various Kinks and Convolutions.—Here are included mixed forms, in which some of the adhesions may form veritable bands, and the predominant factor constituting

strangulation remains doubtful. Cases III. (Fig. 2), V. (Fig. 4), X. (Fig. 5), and XXII. (Fig. 11).

It is not always easy to ascertain the nature of the constricting causes since they may give way during manipulation, and their subsequent identification may then be difficult and perhaps not even desirable. Amongst them omental tags occupy a prominent place, more especially when the lesions are multiple. Again, a band may originate from the tip of the appendix or from the tip of a Meckel's diverticulum, or from appendices epiploicæ, and probably really represents an adhesion which has tailed out. Intermediate phases of a similar kind are frequent in adhesive peritonitis. We require information from the post-mortem theatre as to the frequency with which these bands and adhesions turn up unexpectedly and symptomless. On one occasion, Table II., Case B, where a diagnosis of internal strangulation had been made, there being no external evidence of protrusion, the laparotomy discovered a long fibrous cord passing towards the left iliac region; this was divided and a Richter's hernia was brought into view. On further examination this filamentous cord, about 5 in. long, was found to spring from the anti-mesenteric margin of the ileum 4 in. from the hernia. There being no direct evidence after its division that this cord certainly acted as the source of strangulation, or that the entrance to the femoral canal had not harboured the hernia, this case has been regarded as doubtful and is therefore relegated to Table II.

The constricting causes then may vary in kind and number. That they may be multiple one is apt to forget.

The site commonly affected is admittedly the terminal portion of the ileum. This was definitely ascertained to be so in 15 of the 23 cases. It is natural to expect that the anatomical relations and functional activity of this region should favour such a localisation, and they may even account for the predilection exercised by omental tags. It is also somewhat surprising that many of the flimsy and slight adhesions which give way so readily during operative manipulation should have resisted the distension and violent peristalsis they provoked. It is conceivable that they do occasionally yield without external assistance.

Treatment in the face of such diverse local and general conditions may be simple, as when the mischief is already rectified by the mere handling during operation; but again

it may be complex, involving a hazardous enterectomy. The guiding principles are sufficiently clear. They include removal of the constricting cause, emptying the distended gut, promotion of the intestinal flow, combat of the pathological changes. Individual difficulties must be solved according to the special needs of each case. As in most operations on the alimentary tract, the stomach can be washed out if advisable, and general or local (novocain) anæsthesia employed. The incision, sub-umbilical, may reveal the presence of peritoneal effusion, in amount and character of diagnostic and prognostic value. Escape of distended bowel should be avoided and the whole hand introduced to search for collapsed bowel. If this be found a loop should be withdrawn and carefully followed to the site of constriction. Failing a speedy detection of empty gut the cæcum should be sought, the ileum identified and traced upwards. It may be requisite to enlarge the incision and aid palpation by inspection.

If definite bands are encountered it is well to divide them between two fine forceps and thus settle their anatomical bearings.

The appropriate treatment of A, the local damage at the seat of constriction, and B, that of the general toxæmia and its accompanying evils wrought by the pent-up fermenting contents within the proximal bowel presents problems difficult to solve. The latter condition is the more serious.

The vitality of the bowel concerned is of prime consideration. On this hangs the weighty decision of enterectomy. A careful scrutiny of the constricted zone is essential. If this be of greyish hue, broader than a pack thread, thinned internally, limp owing to loss of tension, it is suspect as liable to perforation and so demands excision. Perhaps a protecting inversion layer of Lembert's sutures might on occasion suffice. Had the need of this been recognised, the perforation, which carried off Case XXIII. (Fig. 12) on the tenth day, might have been averted.

The condition of the distended gut above the obstruction next demands attention. It may be quite paretic, yet the mechanical rush of the pent-up contents into the collapsed bowel on liberation of the constriction may so closely simulate active peristalsis that serious error may arise. Should this paretic bowel not recover tone, subsequent operations of the nature of enterostomy or enterectomy may become obligatory,

possibly with the sad termination experienced in Case XXI. (Fig. 9).

Adhesions, kinks, and twists generally admit of gentle separation and dissection, unless it be judged necessary to excise a matted convoluted area by enterectomy (Case XX., Fig. 8).

Distension of the bowel must be relieved before the abdomen is closed. On division of the constricting agent this may take place spontaneously into the empty portion (Case XV., Figs. 16, 17). When no such gratifying and satisfactory event ensues, the case is one of great anxiety, and various other expedients require to be selected. They have a common object in view, to relieve the distended bowel and to remove all non-viable structure. Thus if enterectomy with primary suture be adopted—and out of eight such operations only two met with success (Cases VI. and XX.)—it is essential to empty the distended gut with suitable precautions, and this was always carried out before effecting union. Or, after the excision, suture may be postponed and the divided lumina provisionally drained externally by means of Paul's tubes; or again, with the upper end so treated, the lower may be closed and returned in the hope of a later secondary union. If enterectomy be not clamant, efficacious relief of distension may be sought by enterostomy (Witzel's valvular method). Enterostomy may also be selected as an adjuvant to enterectomy and also proves helpful in post-operative distension. In like fashion Meckel's diverticulum or the appendix may be utilised for intestinal drainage or as an adjuvant to enterectomy, although in the latter instance we do not for obvious reasons expect the amount of benefit so frequently experienced after colon resections. The bowel content has also been withdrawn by trocar and cannula or incision (enterotomy), the puncture being stitched over and the gut returned.

Local infection during enterectomy is largely prevented if after division of the gut between two closely applied clamps, the central end be gradually withdrawn, as its mesentery is being severed, over the side of the abdomen. The clamp may be then removed, or the gut opened and its contents thus discharged well away from the field of operation; as also the removal of a sufficient length of unhealthy bowel secured. Enterostomy requires careful manipulation to avoid local soiling, but once completed the long tube permits safe drainage. In

both cases gentle compression of the upper abdomen and massage favours escape of the fæcal content. An enterostomy, too, is readily at once converted into an enterectomy by withdrawal of the tube and closure of the bowel with a couple of sutures. It is a more desirable procedure than the use of trocar and cannula or aspiration.

After-treatment proceeds on familiar lines; intraperitoneal, intravenous, or rectal administration of saline solution is generally indicated.

The operation mortality after internal strangulation is very high. It is determined chiefly by the state of the patients on admission, and is therefore largely a matter of chance. These unfortunates arrive exhausted by suffering and transit. They may be already almost *in extremis*, weakened by toxæmia and threatened with pulmonary congestion. Still, no matter how desperate their case, the one way of escape admits of no refusal; operation must be faced. It is depressing to observe that only 12 of the 23 cases in Table I. recovered. However, while out of the first twelve patients only five survived, it is comforting to note that of the second eleven seven got well—a seeming improvement. All three in Table II. recovered.

The appended tables furnish all the data that have direct bearing on the clinical histories. Several post-mortem examinations were obtained, frequently revealing evidence of marked sepsis, and occasionally of peritonitis, as duly recorded. The after-history of the survivors, as far as can be learned, has been uneventful.

There were 15 male and 8 female cases. The average age was forty and varied from thirteen to sixty-eight years.

The illustrative figures are taken from drawings and preparations made directly after operation. The mesenteries have been largely sacrificed in order to gain clearness.

Table II. contains 3 cases somewhat aberrant in character and symptoms, and therefore excluded from Table I.

References to literature may be found in *Deutsche Chirurgie*, Lief. 46 g.; *Der Ileus* by Wilms; in Barnard's *Contributions to Abdominal Surgery;* and in Treves' *Intestinal Obstruction.*

TABLE I.

Case.	Name.	Age.	Date of Admission.	History.	Condition on Admission.	Anæsthetic and Operation.	After-Progress and Result.
I.	Miss C. L.	59	4.1.01.	8 days; sudden colic and vomiting; since last night vomit has fæcal odour.	Very ill.	C. Blood-stained fluid escaped; band near ileo-cæcal junction; contents of distended gut evacuated and washed out; enterostomy.	Died within 6 hours.
II. (Fig. 1)	H. D. .	14	17.1.04.	Sudden complete obstruction, 24 hours' duration.	Distended.	C. Blood-stained fluid; mesenteric band near ileo-cæcal junction; enterectomy; lower end closed; upper drained by Paul's tube.	Died, 18.1.04. Sectio; broncho-pneumonia.
III. (Fig. 2)	R. B. .	27	21.3.08.	5 days; complete obstruction 3 days.	Very ill.	C.E. Mesenteric band and twist, 10 in. from ileo-cæcal junction; resection, 4 ft; end-to-end union.	22nd, vomiting; gastric lavage. 23rd, enterostomies; 2 tubes in ileal coils. Died, 23.3.08. Toxæmic changes in liver and kidneys; distended jejunum.
IV. (Fig. 3)	Mrs M. C.	51	14.7.08.	5 days' complete obstruction.	Much distended; tender right iliac region.	C.E. Fluid; mesenteric band near ileo-cæcal junction; ileum distended; lymph covered; enterostomy.	Died. Sudden syncope, 20.7.09. Sectio; congestion of lungs and pleurisy; extremely fatty dilated heart.
V. (Fig. 4)	A. J. .	26	20.12.08.	5 days' complete obstruction; patient stoutly denies any previous abdominal ailment.	Rigid, tender abdomen.	C.E. Cord-like constricting band springing from small intestine, 32 in. from ileo-cæcal junction, strangulating a mass of adherent convoluted coils of ileum; enterectomy; 2 ft.; end-to-end union.	Died. Passed flatus; sectio; general firm old peritoneal adhesions; cloudy swelling and congestion of kidneys.

VI.	R. W. .	46	26.9.08.	5 days' obstruction. 3 years ago colic, vomiting and diarrhœa for 5 weeks. 7 weeks ago a somewhat similar attack.	Very ill; lies with knees flexed; distended; borborygmi, splashing; gastric lavage gave fæcal-swelling result.	C.E. String-like band from mesentery to same mesentery; enterectomy; 14 in.; end-to-end union.	Recovered, 14.10.08.
VII.	D. G. .	18	23.11.08.	3 days' obstruction.	Tender umbilical and right hypochondrical regions.	C.E. Fluid; band from Meckel's diverticulum to mesentery; flakes of lymph on distended gut; diverticulum utilised as enterostomy drain.	25th, stump closed and returned. Recovered, 13.12.08.
VIII.	C. M'D. .	20	12.4.09.	Sudden pain in right iliac region; obstruction and vomiting.	Rather collapsed.	C. Incision over appendix; early peritonitis and empty ileum; mesial incision; band constricting jejunum divided; enterotomy; evacuation of undigested food; closure of bowel.	Recovered, 30.4.09.
IX. (Fig. 13)	F. M.	31	29.5.11.	Fall from ladder on previous day followed by cramp-like pain in lower abdomen. After a short rest in bed resumed work for 2 hours when vomiting and colic came on. 1905, in Glasgow Western Infirmary, during an attack of "fever" required laparotomy; mesial scar.	Doubled up with pain and vomiting; lower abdomen tumid and rather fixed; pain and tenderness from umbilical region downwards.	C.E. Ileal constriction with adherent omental tags; gut above greatly distended; enterectomy; 12 in.; end-to-end union.	30th, still distended; reopened; 2 enterostomy tubes inserted. 31st, restless; trying to sit up in bed; fell back dead. Died. Sectio; general distension of bowel except in vicinity of enterostomies.
X. (Fig. 5)	W. W. .	68	11.3.12.	2 days' pain and vomiting with fæcal odour; obstruction. For last 12 months diarrhœa.	Abdomen tender; splashing.	C.E. Last 8 in. ileum empty; flattened and plastered against posterior pelvic wall; kinked by adhesions; adhesions freed; appendicostomy.	Recovered, 25.3.12.

TABLE I—*continued.*

Case.	Name.	Age.	Date of Admission.	History.	Condition on Admission.	Anæsthetic and Operation.	After-Progress and Result.
XI. (Fig. 6)	A. H. .	62	15.4.12.	3 days' colic and vomiting; constipated for 1 year.	Very ill; abdomen tender.	C.E. Last 4 ft. of ileum empty, then a constriction, followed by 3 ft. of greatly congested bowel; then a second constriction, and above it bowel more distended and congested; a third constriction due to an omental band at a still higher portion. Enterostomies; 1 tube in jejunum; 2 in ileum.	Died, 16.4.12.
XII. (Fig. 14)	Miss R. .	49	14.5.12.	2 days' obstruction. In Dec. 1911, suffered from colic and vomiting ascribed to retroverted uterus and menopause. In Jan. 1912, had abdominal pain.	Distended.	C.E. Two constrictions due to omental tags, the lower 12 in. from ileo-cæcal junction causing complete strangulation; a second on the distended gut higher up. Enterostomies; 2 tubes in ileum and appendicostomy drainage.	Tubes removed, 20th. Recovered, 4.6.12.
XIII.	Mrs M. M.	40	18.9.12.	5 days' colic and 4 vomiting, latterly with foul odour; had left ovary removed in May.	Umbilical area tender.	C.E. Loop of ileum adherent at base laterally; also at its apex to the bladder.	Recovered, 8.10.12.
XIV. (Fig. 15)	Mrs B. .	48	18.11.12.	4 days' obstruction; had ovary removed 8 years ago and operation for strangulated hernia 4 years ago.	Prominent tender epigastric area.	C.E. 12 in. from ileo-cæcal junction; ileum constricted by a band and adherent to the old mesial laparotomy cicatrix.	20th, bowels acted; 21st, diarrhœa and pneumonia. Died, 22.11.12. Sectio; double septic pneumonia and pleurisy; cloudy swelling of liver, kidneys, and myocardium.

XV. (Figs. 16 and 17)	Miss G. .	21	21.2.13.	From twelfth intermittent colic and constipation, then 3 days' obstruction.	Vomiting less and passage of some flatus.	C. 24.3.13. Band from epiploic appendage above cæcum to ileal mesentery; last 12 in. of ileum beyond constriction collapsed.	Recovered, 14.3.13. 1922, excellent health.
XVI. (Fig. 18)	T. C. .	64	12.7.13.	4 days' obstruction; has become thinner during last year.	Sunken, emaciated; foul-smelling vomit; ladder patterns; splashing.	Local; novocain. Band ruptured in region of right iliac fossa; enterectomy; lateral union.	Died within 10 hours; sectio; hypostatic pneumonia; liver and kidneys fatty; one or two calcified lymphatic glands
XVII.	R. H. .	25	31.8.14.	12 hours' obstruction; appendicitis 4 years ago; of late subject to colic.	Distended abdomen; splashing.	C.E. Band from cæcum constricting ileum.	Recovered, 16.9.14. 1922, excellent health.
XVIII.	Mrs T. .	40	5.6.14.	24 hours' obstruction; vomiting; fæcal odour; had slighter attack one year ago.	Sunken aspect; distended abdomen.	C. Loop of ileum adherent to a calcareous gland and kinked.	Recovered, 24.6.14.
XIX. (Fig. 7)	E. A. .	41	11.10.15.	12 hours' obstruction.	Supra-pubic region slightly tender; splashing.	C. Fluid; omental band passing to posterior pelvic wall.	Recovered, 13.10.15.
XX. (Fig. 8)	A. B. .	16	22.3.16.	4 days' colic and vomiting; 2 days' obstruction and vomit with fæcal odour. Laparotomy for tuberculous peritonitis when aged 2 years.	Patterns; borborygmi; splashing.	C. Last 24 in. of ileum collapsed, matted, adherent and kinked; caseating glands throughout; mesentery; ileo-cæcal enterectomy; lateral union.	Recovered, 6.4.16.

TABLE I—*continued.*

Case.	Name.	Age.	Date of Admission.	History.	Condition on Admission.	Anæsthetic and Operation.	After-Progress and Result.
XXI. (Figs. 9 and 10)	Miss A. S.	63	12.8.18.	24 hours' obstruction; 4 years ago somewhat similar attack; habitually constipated; has taken magnesia for 40 years.	Deeply under influence of morphia; distended; ladder patterns; splashing.	C. 5 in. from ileo-cæcal junction a knuckle of ileum strangulated by a band passing from the appendix. A second constriction (omental) on ileum in Pouch of Douglas; constriction freed; contents of bowel passed onwards freely.	At night still distended; enterostomy. 14th, again ill; second enterostomy; progressed well till 29th. 30th, enterectomy; 20 in. end-to-end suture. Died, 31.8.18.
XXII. (Fig. 11)	R. M.	15	19.3.19.	Since Oct. 1918 attacks of colic, but did not cease work till to-day. 25.9.18, appendix removed; adhesions; pus.	Doubled up with pain; vomiting; very tender below navel.	C. Last 9 in. of ileum with kinks, adhesions, and a constricting mesenteric band.	Recovered, 11.4.19.
XXIII. (Fig. 12)	G. C.	58	24.3.19.	7 days' obstruction; vomit with fæcal odour.		C. Fluid; ashen grey constriction 3 ft. from ileo-cæcal valve; omental? Contents of bowel rushed on freely.	Did well till 27th, then became restless. Died, 29.3.19. Small perforation at site of constriction; peritonitis.

TABLE II.

Case.	Name.	Age.	Date of Admission.	History.	Condition on Admission.	Anæsthetic and Operation.	After-Progress and Result.
A.	Mrs M. .	44	5.3.12.	8 days' colic; doubled up; vomiting; latterly 3 days' diarrhœa.	Tender iliac and supra-pubic regions; bronchitis.	C.E. Broad band passing from pelvic colon deeply.	Recovered, 25.3.12.
B.	Mrs P. .	26	2.6.12.	In Feb. doubled up with sudden acute pain and vomiting for 3 hours. Similar attacks next day, and at beginning and middle of May. The present one began on 29th May.	Distended; ladder patterns.	C.E. Thin band found passing to distended and collapsed gut divided, and a Richter's hernia pulled out, probably from vicinity of femoral ring.	Recovered, 21.6.12.
C.	J. B. .	25	16.7.14.	For 4 years symptoms indicating duodenal ulcer; coffee-ground vomit with blood.	Epigastric tenderness; free HCl.	C.E. 20.7.14. Stomach, pylorus, and duodenum normal; the jejunum was crossed and compressed 4 in. from its origin by a fibrous adhesion-like band; divided; posterior gastro-jejunostomy beyond it.	Recovered, 9.8.14.

DESCRIPTION OF ILLUSTRATIONS

FIG. 1, Case II.—Band seen divided close to ileo-cæcal junction.

FIG. 2, „ III.—Twist and kink of mesentery. A narrow Meckel's diverticulum appears beyond the site of constriction.

FIG. 3, „ IV.—Divided band, one extremity seen on mesentery.

FIG. 4, „ V.—Band with bifurcate base at site of constriction. Stump of a second seen on ileum beyond.

FIG. 5, „ X.—Ileal adhesions plastering ileum against pelvic wall, producing kinks and obstruction.

FIG. 6, „ XI.—Three constrictions, the upper caused by an omental band, the two lower probably from a similar although unascertained cause.

FIG. 7, „ XIX —Coils of ileum constricted by omental band passing to region of posterior pelvic wall.

FIG. 8, „ XX.—Adhesions and kinks causing obstruction.

FIG. 9, „ XXIA.—1. Knuckle of ileum constricted by a band continuous with the vermiform appendix.
2. Second constriction probably omental on paretic distended ileum withdrawn from Pouch of Douglas.

FIG. 10, „ XXI.—Relation of parts in same case after removal of looped band which passed from appendix to adjacent coil of ileum.

FIG. 11, „ XXII.—1. Mesenteric band, adhesions, and kinks.
2. From same case. Bulbous, thick-walled appendix with extremely narrowed lumen, removed six months previously It lay amidst adhesions and a little pus.

FIG. 12, „ XXIII.—1. Constriction, probably omental. The patient died from perforation ten days after operation.
2. External aspect of gut, showing oblique line of former constriction indicated by a white line of lymph and dark perforation.
3. Internal aspect. Two lymph nodules and perforation.

FIG. 13, „ VIII.—Omental tags attached to constriction, also of probable omental origin.

FIG. 14, „ XII.—Two constrictions due to omental tags.

FIG. 15, „ XIV.—Constriction. Probably due to omental tag.

FIG. 16, „ XV.—Band passing from epiploic appendix to mesentery.

FIG. 17, „ XV.—The same after division, showing terminations of band and the collapsed empty gut at once distending and becoming vascular.

FIG. 18, „ XVI.—Band passing from intestine to mesentery, with kink.

Discussion.

Sir Harold Stiles thanked Professor Caird for his most instructive paper and for the admirable diagrams which gave such an excellent idea of the conditions met with at the operations. He emphasised the great importance of early diagnosis in such cases, and urged that the practitioner should not wait until he had become sure of the diagnosis, because by that time secondary changes would probably have occurred which were responsible for the high mortality. He advised that the surgeon be called in as soon as ever the symptoms pointed to the possibility of an acute strangulation, and that in cases of doubt an exploratory laparotomy should be performed. Cases were not infrequently met with in which, after the strangulation had been relieved, some doubt remained as to whether the dilated bowel should or should not be emptied before closing the abdomen. When in doubt he preferred to make one or more enterotomy openings. He asked Professor Caird what he considered the best method of doing this so as to reduce to a minimum the chances of soiling the peritoneum. Sir Harold Stiles said that he had no hesitation in opening the bowel in two or three places, choosing dilated coils which had a long enough mesentery to allow them to hang over the lumbar region well away from the peritoneal cavity while the contents were escaping. It was sometimes an advantage to tilt the patient over towards that side. He thought this a safer plan than the method of threading the bowel over a long glass tube.

Mr Wilkie said we have been privileged to listen to an exposition of a subject of rare intricacy and of absorbing interest by one who speaks with great authority. Few surgeons have enjoyed the wide and diverse experience which has been Mr Caird's. Still fewer have, with a wide experience, combined that instinct of the surgical pathologist which he possesses in such a singular degree, and have that passion for immediate and accurate record of conditions found; and probably no other has, with all those, possessed that artistic talent and faculty for graphic portrayal which give to Mr Caird's communication a unique distinction. The classification of acute obstruction on a broad pathological basis must necessarily be into cases in which merely the onward passage of the intestinal contents is interfered with and those in which, in addition, the blood supply of the intestine is compromised, *i.e.*, into simple obstruction and strangulation. In the former the gravity of the case will depend on how high up in the intestinal tract the obstruction occurs. Rapid poisoning and great loss of fluid characterise the higher obstruction, slowly increasing toxæmia the lower. In strangulation the factors of shock and devitalisation of tissue with consecutive infection will play a leading rôle. Possibly the question most in dispute will be the advisability

of emptying the distended gut above the obstruction at the time of operation. This immediately raises the question, What is the poison which is likely to be absorbed from the distended gut? The work of Draper, Whipple, and the Dragstedts has shown that the poison is of the nature of a proteose. Now the only proteolytic ferments in the intestinal tract which can break up protein into proteose are those of the gastric and pancreatic secretions; the erepsin of the succus entericus converts the proteose into amino-acids but cannot break up protein. It is obvious that intoxication with proteoses is more likely to occur in the higher reaches of the intestine, duodenum, and upper jejunum. It is when obstruction lower down tells back on this high "poisonous proteose level" that serious toxic symptoms supervene. Consequently it is when this high level is the seat of distension and stasis that measures for emptying it must be seriously considered. In the less severe cases merely milking its contents downwards into the gas-filled ileum will be sufficient if energetic post-operative treatment is adopted. In late cases an enterotomy, or preferably an enterostomy, will be indicated, and in either case the drainage must be directed to the high jejunal coils. In the class of case where the viability of the bowel at the seat of compression by band or adhesion is doubtful, the method introduced by Mr Caird many years ago of simple invagination by Lembert sutures is usually sufficient and few simple surgical devices have saved so many lives.

Mr Caird stated, in response to Sir Harold Stiles and Mr Wilkie, that he referred in his written communication more fully to the points they had raised. He agreed with Sir Harold Stiles that methods of emptying the full bowel after enterectomy and prior to suture, by introduction of long rigid tubes, did not commend themselves. Enterotomy and enterostomy required especial care by packing off to avoid peritoneal contamination. It was difficult to dogmatise as to the best treatment of paralytic ileus from such a relatively small number of cases. The surgeon must settle that from the problem presented.

PRIVATE BUSINESS.

The following were elected members of the Society: George Morris, M.B., Ch.B., D.P.H., Hugh S. Davidson, M.B., Ch.B., F.R.C.S., and W. F. Theodore Haultain, M.B., Ch.B. (Cantab.).

THE PROTECTION OF MANKIND AGAINST TUBERCULOSIS.

*Being an Address before the Medico-Chirurgical Society of Edinburgh.**

By Professor A. CALMETTE, Institut Pasteur, Paris.

Ladies and Gentlemen,—Allow me, in the first place, to express my profound appreciation of the honour your President has done me in inviting me to visit the illustrious University of Edinburgh, and to address an audience animated by the noble feelings of altruism which have in all times characterised your scientists and the people of Scotland.

It is with lively emotion that I visit this modern Athens, the country of Walter Scott and of so many personalities celebrated in all the manifestations of human intelligence. In welcoming me here so cordially you have wished, I feel sure, to testify to your love for my country which is united to yours by so many ties that link our souls, and you may have wished also, in this the Centenary of Pasteur, to honour one of the disciples of the master to whom humanity owes so many benefits. I thank you for your kindness.

Sir Robert Philip has made me hope that you would gladly listen to a short exposition of the present state of our knowledge regarding immunity against tuberculous infection. I therefore pass at once to the subject which occupies the attention of the bacteriologists of every nation in the civilised world.

After his demonstration of the specific character of the tuberculous virus and its inoculability to different animal species, Villemin, finding it difficult to transmit tuberculosis to the dog, the cat, and the sheep, was the first to raise the question whether animals existed which were non-sensitive to this disease.

Later, after the discovery of the tubercle bacillus by Robert Koch, we learned that almost all the mammalia could be artificially infected, but that a small number of species had the grim privilege of contracting tuberculosis spontaneously, and that some others were so highly resistant as to be immune even to artificial inoculation.

* Delivered 7th June 1922.

For example, there exist in the desert of Sahara and also in the steppes of Southern Russia certain rodents, the *gerbilles* (*Meriones shavii*) and the *spermophiles* (*Spermophilus citellus* or *fulvus*) into which tubercle bacilli can be injected subcutaneously without any effect, save a local lesion which has no tendency to become generalised and which causes no serious functional disturbance.

These non-tuberculisable animals are thus *naturally resistant.* Tubercle bacilli remain within their fluids or tissues as inoffensive foreign bodies. Yet the bacilli escape digestion by the leucocytes which have absorbed them. The animal succeeds in getting rid of the bacilli very slowly. It eliminates them gradually by way of the natural discharge of cellular waste. But for months, even for years, they may be traced round about the point of inoculation where they preserve their vitality and virulence. For they are perfectly capable of tuberculising other susceptible animals such as the guinea-pig.

It is the establishment of a tolerance of this kind which must be our aim in the production of *artificial immunisation.* It would indeed be vain to hope to be able, in the case of animals susceptible to tuberculous infection, to confer the power of digesting tubercle bacilli when animals naturally resistant to the disease cannot do so. The chitinous membrane containing waxy and fatty substances which envelops the toxic and toxigenous protoplasm of these bacilli constitutes such an obstacle to the digestive action of the leucocytes, that we cannot conceive antituberculous immunity as resulting from a process analogous to that which occurs in the case of immunity to the acute infectious diseases—a process characterised by the formation and rapid massive circulation of *antitoxins* and of *bacteriolysins* in the fluids of the body.

The problem may be put therefore as follows:—How to render the leucocytes and the endothelial cells of the vessels—which enclose the tubercle bacilli but are unable to digest them—how to make these cells non-sensitive to the poisons which these bacilli contain and secrete (endo- and exotoxins) so that the organism may tolerate them as it can tolerate in most of its tissues the presence of a number of inoffensive foreign bodies such as particles of silica, carbon, or metallic fragments even of considerable size.

When Robert Koch—some thirty-two years ago—prepared his first tuberculin he believed, and the whole world hoped, that

this purpose had been attained. Those of us who were then doing laboratory work will never forget the immense enthusiasm which was aroused by the announcement, nor the cruel disillusionment which followed.

A specific cure for tuberculosis had not been found, but Robert Koch had observed a fact of capital importance, namely, that tubercle bacilli, whether living or killed by heat, act very differently *according as they are introduced subcutaneously into a tuberculous guinea-pig or into a healthy guinea-pig.*

While, in the case of the *healthy* guinea-pig, they give rise only after several days to the formation of a nodule which discharges externally, causing an ulcer which may continue till the death of the animal and which leads to intense swelling of the neighbouring lymphatic glands, a similar inoculation in the case of the *tuberculous* guinea-pig produces a small abscess which quickly bursts and discharges and cicatrises without swelling of the neighbouring glands.

This *phenomenon of Koch*, the importance of which from the point of view of immunity to tuberculosis had apparently escaped Koch's attention, affords evidence of the *intolerance of the tuberculised individual to fresh infection.*

Experiments show that this intolerance becomes more and more marked, and reveals itself by an effort to expel the bacilli which is more intense and more rapid with *each fresh reinfection.*

This is then exactly the reverse of what ought to be realised in a true *vaccination against tuberculosis.* We shall see, however, that it is possible to obtain therefrom useful guidance and an advantageous outlook in the practical direction of the social campaign against tuberculosis.

Thanks to the local tuberculin reaction which has been used so largely for a number of years, especially in children, for the earliest possible diagnosis of bacillary infection, the conviction has been forced on us that bacillary infection is almost inevitable in the course of childhood, especially in our crowded city areas.

At five years of age 6 per cent. of children, apparently quite well, are already affected, and when the age of fifteen is reached the proportion rises to 90 per cent. It is thus very exceptional for the individual to reach adult age and escape every chance of infection.

On the other hand, we all know that mortality from tuberculosis is extremely frequent in young life. In the Paris hospitals,

of 100 children dying in the course of the first year of life, 28 deaths are due to tuberculosis, and of 100 deaths of children during the second year, 26, while for children whose ages range from three to fifteen years the collective percentage of deaths from tuberculosis does not exceed 7.

It is thus *in earliest infancy* that household contagion, which is almost inevitable for babies born of phthisical mothers, is most serious and most generally fatal, because it is *massive* and *repeated day by day*. After the third year such infection is less formidable. Then it is occasioned by accidental exposure and intermittent contact, which produce more often glandular lesions of benign character very frequently curable, and induce that characteristic state of *intolerance of fresh infection* shown by the tuberculous patient.

In animals experimentally inoculated, the same facts are observable. Young bovines, for example, recover almost always when care is taken to isolate them after they have on one occasion ingested virulent bacilli. On the contrary, they never recover, and become rapidly tuberculous when they are inoculated several times at short intervals, or when they are left in prolonged contact with other tuberculous animals.

It seems then that for man, as for animals which develop tuberculosis spontaneously, such as the bovines, one early and slight inoculation is desirable, provided that it is not followed by further *repeated*, *massive* infections. Such slight inoculation confers on the organism a resistance which, while not a true immunity, protects it in case of subsequent reinfections of grave character from developing the disease in rapidly fatal form. It may be affirmed that *every subject infected in childhood by a very feeble dose of bacilli is rendered less likely to contract acute miliary tuberculosis.* Should the individual be exposed later to repeated or massive contagion, he will show his intolerance to reinfection by developing chronic tuberculosis (phthisis) or cold abscesses or other local tuberculous lesions which suppurate readily.

There can be no doubt that the glandular system, especially developed in youth, affords an effective barrier to the rapid invasion of the organism by the tubercle bacillus. Likewise, *slight infections*, *not repeated*, tend to be benign in the case of children, while, contrariwise, they are grave in the adult who has remained virgin soil in respect of bacillary implantation. This is why country people who, after adolescence, have migrated

to the city, develop so often a serious type of tuberculosis, it may be, rapidly fatal. It explains similarly why negro races coming from the centre of Africa, where tuberculous infection has not yet penetrated, are so sensitive when they are transferred to a European country, where it is difficult for them to escape opportunities for infection.

Long before the part played by reinfection was understood as it is to-day, we had already sought to realise immunity to tuberculosis by the use of the Pasteurian method of attenuation of the virus, or the method of vaccination by soluble toxins produced by the bacilli in culture mediums—methods based on the work of Roux and Yersin and later of Behring regarding diphtheria toxins and antitoxins.

These attempts, although for the most part fruitless, have taught us at least to recognise the kind of reaction shown by organisms sensitive to tuberculous infection in respect of bacilli of different types and in respect of products derived therefrom.

In the first place, attempts were made to use tuberculins and bacillary extracts as a vaccine. But these substances which are hardly toxic for healthy subjects are incapable of conferring appreciable resistance on animals which are afterwards inoculated with bacilli.

Next, one turned—with more encouraging results—to living bacilli more or less modified in their virulence, or passed through different animal species.

The attempts of Behring to vaccinate young calves by intravenous inoculation with bacilli of human type occupied for long the attention of biologists. This "jennerisation" of cattle, as it was called, became, in 1902, the subject of numerous observations and important applications among cattle, particularly in Germany, Hungary, Denmark, Sweden, Italy, France, and the United States. It was possible to conclude that the bovovaccin of Behring confers on young calves an appreciable resistance to different modes of natural and artificial infection, but that this resistance—of brief duration, not exceeding twelve to fourteen months—evidenced while it lasted by the more or less complete absence of tuberculous lesions, does not allow the organism to absorb test bacilli of virulent character nor even those introduced as vaccine. These bacilli one and all are retained at least in part during months in the lymphatic glands, and continue there ready to show more or less abruptly their

presence by anatomical disturbance so soon as the resistance artificially conferred by the vaccination begins to give way.

It was established, on the other hand, especially by the researches made in England by A. Stanley Griffith, that vaccinated animals eliminate for a long time in intermittent fashion in their excreta, and milch cows especially by way of the mammary gland, tubercle bacilli which have the characters of the human type. Such elimination evidently entails grave risks which have led to the complete abandonment of the method.

Similar disadvantages have led to the rejection of the analogous method proposed by Robert Koch who used a bovine bacillus of slight virulence, and that proposed by Arloing (of Lyon) who availed himself of a human bacillus in homogeneous culture, and that proposed by Theobald Smith who gave to cattle, in one intravenous injection, 1 to 2 milligrams of a culture of bovine bacillus attenuated by age.

Several observers have preferred to avail themselves of the avian bacillus. But apart from the fact that that bacillus is virulent for certain mammalia, especially the pig, horse, rabbit, and sometimes man, it did not seem to confer appreciable resistance in respect of human or bovine bacilli.

Recently there has been a good deal of talk in Germany regarding the attempts of Friedmann by means of an acid-fast bacillus isolated from the tortoise in the Berlin Aquarium. Not only was the claim to preventive vaccination made, but it was even affirmed that injection of that microbe was of curative value in tuberculosis. It did not require very long before it was proved that there was nothing in it, and the so-called Friedmann cure was speedily abandoned.

Some degree of hope was also placed on the sensitisation of living bacilli by means of certain serums rich in antibodies, and obtained from tuberculous animals injected either with dead bacilli or with bacillary extracts. But it was found that the microbes, thus sensitised, in place of vaccinating, produced a more rapid infection than the same bacilli, living but not impregnated with antibodies.

Another attempt, of rather risky character, was made by Gerald Webb and W. Williams, who proposed to inject very small doses of virulent bacilli—*single* bacilli—in such a way as to effect a latent infection analogous to that which is produced spontaneously by slight contagion, and *thus* obtain protection

against reinfection. But this method, which was never practised save in the laboratory, is evidently too dangerous for general use.

A well-known Spanish observer, J. Ferran (of Barcelona), has for a number of years made investigations on vaccination by means of an acid-fast bacterium which, according to him, is derived from the tubercle bacillus by a series of successive "mutations." But this bacterium does not lead in the organism to the production of tuberculous antibodies. We have no proof that it is derived from an authentic tubercle bacillus, or that in the case of susceptible animals it exerts an effective protection against a virulent infection. We cannot at the present time pass any judgment on the attempts made directly by J. Ferran in the human subject.

Following observations which I had made myself with the collaboration of C. Guerin regarding the modifications undergone by the tubercle bacillus (*in culture*) in its passage through the digestive tract, and thereafter by the implantation in long successive series on an artificial medium containing pure ox bile, I had been able to obtain a growth of bacilli completely free of virulence for the guinea-pig and rabbit, and perfectly tolerated in large intravenous doses—up to 100 milligrams—by the ox and capable of producing tuberculous lesions in the organism.

For several years before the great world catastrophe which stopped all investigation, we had completed observations on the employment of this *non-tuberculigenous* bacillus for the vaccination of calves, and we had obtained some interesting results which our recent work has entirely confirmed and extended. It has now been demonstrated that our bile-treated bacillus, injected intravenously, is inoffensive to all mammalia and never produces tubercle, and that it confers on animals manifest tolerance in respect of infections or experimental inoculations.

Unfortunately it does not seem that this tolerance is of very long duration. In the ox it does not exceed eighteen months. In the rabbit and guinea-pig it seems to last five or six months. It disappears when the vaccinating bacilli have been completely eliminated from the organism, and it continues so long as the bacilli continue their life in the lymphatic cells. There is some hope that the tolerance would be maintained or prolonged by revaccination made at suitable intervals in such a fashion that the production of *Koch's phenomenon* would be avoided, but this possibility has not yet been demonstrated.

It is further very difficult to prosecute these attempts at anti-

tuberculous vaccination in laboratories and in countries where bacillary infection is so widespread that a given animal cannot certainly be protected from accidental contagion. It would be necessary to make the attempt in an environment above suspicion, in a country where there are no men, no cattle, nor other tuberculous animals.

That is why I have proposed the creation of a centre of research in a position as isolated as possible, preferably on the west coast of Africa in the great belts of forests inhabited by large anthropoid apes, especially the chimpanzee.

In such a laboratory one could, for as long as might be serviceable, keep the vaccinated animals in a state of semi-liberty, securing for them in the heart of their native country nourishment and conditions of climate and life generally in conformity with their needs. After a more or less prolonged interval, we should be able to test on the spot their resistance to artificial infection, or they might be transferred to Europe where they would be exposed to natural contagion which so cruelly affects their congeners in menageries.

Without waiting until such a project can be realised, it is our duty to pursue investigations which tend to produce in young animals susceptible to tuberculous infection, and in young children, that particular state of intolerance to reinfections which may result *from the early implantation in the organism of a small number of slightly virulent bacilli, or by bacilli which do not readily produce tuberculous lesions.* It seems that at present this is the way which ought to lead to the most satisfactory results.

And yet, who would dare to say that *Chemotherapy, preventive or curative*—that new science which has resulted from the work of Ehrlich on the treatment of spirilla and trypanosomes by organic arsenical compounds—may not have in store for us happy surprises as regards the prevention of tuberculosis.

There has long been an idea that we might destroy the tubercle bacillus *in vivo* by means of antiseptic agents whose bacteriolytic power was sufficient for the purpose, while leaving intact the cellular tissues of the patient. This hope—which has constantly been disappointed—has led to the employment of creosote, guaiacol, thymol, formaldehyde, sprays of various essential oils, and even aniline dyes. None of these substances introduced either into the blood circulation by subcutaneous or

intravenous injection, or by inhalation in combination with air, reaches the bacilli *within the tuberculous lesion.* The substances are destroyed or decomposed or become fixed in the tissues long before the lesions can be reached.

It is, moreover, chimerical to hope to convey to these lesions by way of the blood, the lymph, or the air, any substances which possess a special chemical affinity either for the bacillus or for the tuberculous cell. It is a failure to recognise the essential fact that the tuberculous cell—which is no longer a normal cell but a new complex produced by the symbiosis of tubercle bacilli and of the elements which constitute the giant cell (just as the lichen is the product of the symbiosis of an alga and a mushroom)—exists independently of the organism which serves as host. The tuberculous cell is no longer linked to its host by any capillary vessel. It becomes more and more isolated in proportion as it tends towards caseation or towards calcification. It is nourished only by way of osmosis, and it is also by way of osmosis that the normal cellular elements which surround it become impregnated with toxic products which it diffuses externally.

It is only possible to conceive of effective action on tuberculous cell formation by a chemical agent, provided that agent possesses in the first place sufficient stability to ensure its carriage without decomposition or modification to the cellular protoplasm which surrounds the tubercles, and provided thereafter it can penetrate by osmosis into the tuberculous cell itself, so as to act on the protoplasm of that cell or on that of the bacilli therein contained.

It is still possible that some chemical substance might exercise an indirect influence on the tubercles by *favouring the transformation into fibrous tissue of the unaffected cells surrounding the tuberculous focus.* It is no doubt in this way that calcium salts act, possibly also various salts of copper and certain iodine compounds. When the fibrous tissue becomes sufficiently dense to interrupt or suppress the process of osmosis, the complete isolation of the tubercle leads to its death and the degeneration of its protoplasmic and bacillary content. Such a curative process is happily of frequent occurrence. It is the rule in cases of discrete tuberculous infection, and is seen sufficiently often even in the case of most susceptible animals such as the guinea-pig, in the event of their inoculation with a few *single* bacilli of slight virulence.

Up to the present, chemotherapeutic attempts have been carried out in rather haphazard fashion whether by phthisiologists directly on tuberculous patients, or by some investigators on animals in the laboratory. And in spite of the efforts which have been made to discover among chemical agents a substance capable of preventing or arresting the evolution of experimental tuberculosis in the guinea-pig or rabbit, the results so far recorded have not been very convincing.

This is no reason for discouragement. In addition to the fact that our knowledge of cellular chemistry is advancing from day to day, we have already attained many valuable conceptions which ought to be serviceable regarding means of increasing the resistance of the organism to attack by the tubercle bacillus.

The most important conception to which I should like, ladies and gentlemen, once more to draw your attention, is that the best safeguard whereby to protect against grave infections is the presence within our lymphatic system of bacillary elements of such slight virulence as will not cause tuberculous lesions, and sufficiently distributed that some of them will remain sufficiently long in our tissues and there establish that particular state of immunity which in tuberculosis implies *intolerance to reinfections.*

The essential aim we must ever have in view is not, as some have supposed, the exclusion of possibility of bacillary contagion, but rather the realisation of contagion in all human beings, *as soon as possible after birth*, in a form which is inoffensive and protective for a sufficiently long time against serious infection. The establishment of such resistance on the part of infants ought then to become the immediate object of our constant endeavour. *The child must be immunised from his earliest age*, firstly, because in infancy it is most exposed, and further, because it is relatively easy to shield it from repeated and massive contagion which irremediably imperils its life.

The practical conclusion which emerges from our present-day knowledge is that our *efforts should principally be directed towards the protection of childhood.*

That protection is realised most effectively in the first place by removing the infants of phthisical mothers separately to healthy households in the country, thus insuring their protection from infective contact during the two first years of life;

next by the removal of families or larger groups of children from three to thirteen or fourteen years to sanitary conditions above suspicion; and finally by the constant surveillance of schools, of apprentice workshops, and food supplies, such as milk, which may contain or carry tubercle bacilli.

One may hope that later, when knowledge has advanced still further, it will be possible to confer on babies, from the moment of their appearance in the world, through the ingestion of, or inoculation with, a certain number of living but *non-tuberculigenous bacilli*, the capacity to resist accidental virulent infection.

The whole world awaits anxiously such a realisation.

Discussion.

Professor Ritchie said they could not but recognise that they had that night listened to a great exposition by a master of a most difficult subject. It was certainly impossible in the present state of knowledge to account for the recoveries from tuberculosis which occur. Tuberculous disease was, however, not the only condition in relation to which the processes underlying recovery and immunity were obscure. In respect of such questions the tubercle bacillus was only a representative of a group of organisms which included the pneumococcus, regarding whose capacity of originating immunity reactions little was known. As he understood it, Professor Calmette's position was that hitherto it had been found impossible to produce experimentally in animals anything more than a transient immunity to or tolerance of the tubercle bacillus. Yet Professor Calmette held that in man the production of an effectively lasting immunity occurred. It seemed necessary to assume this because of the widespread infection which occurs in children, 90 per cent. of whom are said to be infected before the age of 16. Professor Ritchie pointed out that such an assertion largely rested on evidence derived from the application of the tuberculin reaction. He could not bring himself to be satisfied with such evidence unless it was supported by facts derived from the study of morbid anatomy. While a great deal of labour had been devoted to such study, he thought much further work was required regarding the prevalence of tuberculosis before any conclusion as to the percentage of infections in the world's population could be formulated. It was certainly the case that the prevalence of latent tuberculosis varied in different parts of the world. Certain work done in Edinburgh, for instance, did not yield evidence of there being a 90 per cent. infection rate. There were geographical, racial, and social conditions to be studied far more fully than had hitherto been done. Investigations of this kind are beset with very great difficulties but these must be faced. Furthermore, they must be overcome before any procedures for the immunisation of young children can be justified. In these circumstances Professor Ritchie thought it would be well for the medical profession to reserve to itself the knowledge of such immunisation being possible. Already the idea had been publicly mooted that an

infection with tuberculous milk during childhood protects the individual against reinfection in later life. In the light of the present available scientific knowledge there is no ground for such a position.

Professor J. Lorrain Smith said the address to which we have just listened has dealt with the subject of tuberculosis from many points of view. It is based on inquiries into the bacteriology and pathology as well as the treatment of the disease. I may be permitted to refer more particularly to the account of the phenomena which are seen in the process of tubercle. We are accustomed to look on the changes round the seat of infection as evidence of a reaction originally and essentially defensive in nature. Professor Calmette describes the relation of the tissue and the invading bacillus as one of symbiosis. The tuberculous cell is a complex of tissue cell and bacillus which are partners in symbiosis. The complex is in large measure independent of the tissue from which it has originated and of the body which is its host. This symbiotic complex is an aggressive factor in the development of the tuberculous lesion. From this source is derived the toxin which is destructive to ordinary tissue cells in the neighbourhood or in the body generally. The relationship of the tuberculous cell to ordinary tissue cells may be compared with that of the cancer cell to the tissues of its host.

When a tuberculous lesion heals the tuberculous cells are enclosed by a zone of fibrous tissue, or by a deposit of calcium salts, and subsequently perish. This conception of the mechanism of the tuberculous process is at once a stimulus of renewed inquiry, and pathologists will return to a study of the tissue-changes, furnished with a new interpretation of the tuberculous reaction.

May I join in the expression of the pleasure with which we receive Professor Calmette in Edinburgh. From far-off times up to the present there has been close association between the medical schools of Paris and Edinburgh. Developments of teaching and research in Paris have ever had the most direct influence in Edinburgh. I might adduce illustrations of this throughout the history of the Edinburgh School, but I need refer to one only, that association in which the teaching of Pasteur passed to Edinburgh, and in the hands of Lister was worked out as the foundation of modern surgery. Professor Calmette's address is the latest instance of association in teaching and inquiry. It may be shortly described as a programme of research. By the life-work of our President the Edinburgh School has been prepared to take its part in the realisation of the defensive measures against tubercle for which, in the words of the address, the whole world anxiously awaits.

Sir David Wallace, the President of the Royal College of Surgeons, said that he only voiced the opinion of the Fellows of the College in saying that it was a pleasure to place their Hall at the disposal of the Society, and that they were honoured in having such a distinguished scientist as Professor Calmette within their walls. On behalf of the College he extended a hearty welcome to him.

The President, Sir Robert Philip, conveyed to Professor Calmette the sincere thanks of the Society for his address.

THE THERAPEUTIC VALUE OF QUINIDINE SULPHATE IN AURICULAR FIBRILLATION.*

By W. T. RITCHIE, M.D., F.R.C.P.

AURICULAR fibrillation is not only a frequent but also a grave disorder of the cardiac action. When the auricles are in fibrillation the rhythm of the ventricles is wholly irregular. Their output per beat is inconstant, and their rate of contraction is often much accelerated. The condition often causes marked palpitation, the reserve power of the heart is lessened and physical exertion induces a more pronounced acceleration of the pulse and a greater degree of breathlessness than would have been occasioned if the heart's action had been normal. In more grave cases of auricular fibrillation, the ventricles are dilated and signs of more pronounced cardiac failure supervene. When auricular fibrillation is once established in the human heart it usually persists until the end of life. It is therefore evident that any therapeutic remedy would be welcome if, arresting auricular fibrillation, it promoted restoration of the normal cardiac rhythm.

Influenced by the writings of one of our corresponding members, Professor Wenckebach, who had drawn attention to the therapeutic value of quinine in some affections of the heart, Frey tested the action of various cinchona alkaloids in patients presenting auricular fibrillation. His paper published in 1918 showed that the administration of quinidine sulphate might in some instances lead to the restoration of the normal rhythm. His work was followed by that of Levy in 1921, and later by that of Drury and Iliescu, of Ellis and Clark Kennedy, of Lewis and his collaborators, of White Marvin and Burwell, and of many others.

The normal auricular action is stated to have been restored by quinidine in 57 per cent. of over 200 cases. The drug was promptly regarded as of great clinical value. Its action has been acclaimed as one of the most dramatic in the whole realm of functional therapy; it has been claimed to afford relief from the palpitation associated with auricular fibrillation, to improve the general condition of the patients, and usually to obviate the necessity of continuing digitalis.

I have observed the administration of quinidine in 12 cases

* Read 3rd May, 1922.

of auricular fibrillation, eight men and four women. One was a case of exophthalmic goitre; in another, the main clinical condition was that of profound melancholia; a third suffered from syphilitic myocarditis; in 8 there was coincident mitral valvular disease, there being incompetence of the valve in 6 cases and stenosis in 2. The mitral lesion was in some instances of rheumatic, and in others almost certainly of syphilitic origin. In only 3 of these 12 cases was the normal rhythm restored, and in only 2 of these 3 did the restoration persist for any length of time.

Following the original recommendation of Frey, who found that in some individuals various toxic manifestations might be induced by quinidine, it is customary to give an initial, oral, dose of 0·2 gram twice daily. If no idiosyncrasy to the drug be shown, 0·4 gram may then be administered orally three or four times a day. If the normal rhythm is about to be restored this event will probably occur after comparatively few doses of quinidine have been administered. In Case VI. of this series the normal rhythm was regained on the third day, after 2·4 grams of quinidine sulphate had been taken. In Case IX. the normal rhythm was regained on the sixth day after beginning the administration of 0·4 gram thrice daily. If the normal rhythm is not restored after the giving of 0·4 gram six hourly for a week, its administration in more frequent doses or for a longer period is not likely to yield success.

The normal rhythm, once it is restored, is not often maintained for longer than a few hours or days, and the fibrillation then recurs even although the administration of quinidine is being continued. In Case VI. the normal rhythm, reappearing on the third day after 2·4 grams of quinidine, was maintained for three days; on the fourth day, when 1·2 gram of quinidine was administered the fibrillation was resumed and persisted for twelve weeks despite the administration of quinidine in doses of 0·2 gram thrice daily for twenty-five days, and of 0·4 gram. six hourly for six days. In Case IX. the normal rhythm, regained on the sixth day after a full dose had been begun, was preserved for a week, and for six days after the administration of quinidine had been stopped. In another case (No. VIII.), after 0·4 gram of quinidine thrice daily for six days, the normal rhythm was regained, but this was interrupted by extrasystoles which recurred in series at a rate of 146 to 150 per minute. The quinidine was discontinued; four days later the auricles were

again fibrillating; digitalis tincture was then administered daily, and ten days later the normal rhythm was restored and it has been well maintained for six weeks, the patient meanwhile taking 30 minims of digitalis tincture and 0·4 gram of quinidine sulphate daily.

If the drug has proved successful in a given case it seems likely to prove equally successful on a subsequent occasion.

In successful cases, the first effect of quinidine, as determined electrocardiographically, is a slowing of the rate of the auricular deflexions; coincidentally the rate of the ventricular contractions may increase. The subsequent sequence of events in successful cases is, fine fibrillation, coarse fibrillation, impure flutter, and flutter, and subsequently, after a short period during which the whole heart stands still, the resumption of the normal rhythm. In unsuccessful cases the fibrillation either persists unchanged or, less frequently the fibrillation, after being temporarily replaced by flutter, recurs. In a given case we cannot foretell whether quinidine will prove successful or will fail. In Case VIII., a man aged 36 suffering from mitral stenosis, auricular fibrillation had persisted for two years, nevertheless the normal rhythm was restored. In Case XII., the man aged 40, was quinidine-proof. He presented mitral stenosis of rheumatic origin and auricular fibrillation of three and a half years' duration, but this had caused less functional incapacity than in the former case.

The observation that the two successes (Nos. VIII. and IX.), the temporary success (No. VI.) and the transient conversion of fibrillation into flutter (No. X.) occurred in non-syphilitic cases, and that failure was observed in the frankly syphilitic cases should not be regarded as an indication of any essential difference between syphilitic and rheumatic cases in their response to quinidine.

What is the action whereby quinidine converts the incoordinate fibrillar contractions of auricular muscle into rhythmic co-ordinate contractions? We could answer this question with greater precision if we knew definitely the nature of the functional disturbance underlying auricular fibrillation. As long ago as 1888 MacWilliam advanced the hypothesis, founded on experimental work, that fibrillar contraction of the ventricles might be due to defective conductivity, namely, to blocking of impulses within the muscle whereby they reach muscle fibres at varying periods. In 1912 I suggested that auricular

fibrillation might similarly be due to defective conduction of impulses within the auricular walls. The effect of vagal stimulation and of digitalis in regard to auricular fibrillation support this hypothesis.

The opinion advanced by Lewis that auricular fibrillation was due to stimuli constantly arising in every part of the auricular wall is now discarded. His recent experimental observations suggest that fibrillation is due, not to delay in the conduction of impulses, but to curtailment of the refractory period of the muscle, and that because of the short refractory period a wave of contraction once initiated circulates continuously in circus fashion. If we accept this opinion the conversion of fibrillation into flutter on the one hand, or into the normal auricular action on the other, is explicable on the assumption that quinidine lengthens the refractory period of the auricular muscle and thus prevents a single impulse from spreading repeatedly and indefinitely throughout the auricular walls. Lewis and his collaborators have also brought forward evidence to show that quinidine depresses conductivity within the auricular walls and paralyses the vagus.

Quinidine causes unpleasant symptoms in some individuals. One man (Case VIII.) stated that he felt as if his heart were going to burst, and again as if a red-hot iron were passing through it; his countenance was somewhat grey in colour at that time, his pulse still irregular, its rate 104. One woman (Case XI.) who was convalescing from severe dropsy and whose auricles were still fibrillating, complained of headache, nausea and faintness, which led to the drug being discontinued. In a third case (Case VII.) an alarming seizure simulating grave syncope gave occasion for much anxiety. A few weeks later when the patient was no longer taking quinidine a similar seizure supervened, but it was recognised to be of frankly hysterical nature.

I have not observed any serious symptoms arising during the administration of the drug, but it is not devoid of risks. During the stages transitional between fibrillation and normal rhythm the ventricular rate, already unduly fast, may be markedly accelerated and the gravity of the patient's condition may thereby be intensified. This unfavourable effect, although by no means common, may be obviated by the simultaneous administration of digitalis. Until recently it was supposed that the actions of this drug were antagonistic to those of

quinidine, and it was recommended that if digitalis had been given it should be discontinued for some days before quinidine was administered. But it is now evident that it is not necessary to discontinue the digitalis and that both drugs may be given concurrently.

A second unfavourable effect of quinidine is the development of multiple ventricular extrasystoles in rapid sequence, constituting an extrasystolic ventricular tachycardia at a rate of 150 to 200 or more per minute. This arose in one of my cases (Case VIII.) and, as it may be the precursor of ventricular fibrillation and therefore of sudden death, this tachycardia was sufficiently alarming to necessitate the discontinuance of quinidine. At a later date the same individual was given quinidine and digitalis concurrently, without any tachycardia arising and with restoration of the normal rhythm. This was interrupted by an occasional auricular extrasystole.

A third and more frequent danger is one which may ensue when the fibrillating and therefore dilated and functionally passive auricles, passing into flutter, begin to contract rhythmically at an extremely rapid rate, 280 to 300 or more per minute, or when they resume their normal contractions. The frequency with which thrombi form within the cavities of fibrillating auricles and the various embolic phenomena which may ensue after portions of those thrombi become detached are well recognised. If the auricles, under the influence of quinidine, begin again to contract, whether they be fluttering or beating with a normal rhythm, there is considerable risk of detachment of portions of thrombi and consequently of cerebral, pulmonary, and renal embolism. It is mainly with this danger in view that patients to whom quinidine is to be administered should be selected carefully. I have never risked giving the drug to patients who presented, in addition to auricular fibrillation, the signs of gross ventricular dilatation as revealed by cyanosis, œdema of the limbs, ascites and pulmonary œdema. In such cases it is advisable to withhold quinidine until the dropsy has been relieved by means of rest in bed, by digitalis or strophanthus, and possibly by diuretics. Not until then should quinidine be given, and the digitalis should be continued meanwhile.

Is quinidine a valuable remedy? The claim that in 57 per cent. of recorded cases the normal rhythm is restored is somewhat misleading. The restoration is often of brief duration,

but in exceptional cases the normal rhythm may be maintained for some months if the administration of the drug is continued in appropriate doses. In only 3 cases of my series was the normal rhythm re-established, and in only 2 of these 3 was the normal rhythm well maintained. Only once (Case VIII.) have I observed any decided improvement in the patient's clinical condition when the normal rhythm was regained. When his auricles were fibrillating this man was breathless and confined to bed. Now, six weeks after the normal rhythm was first restored, he is able to be up nearly all day, his breathing is easier, and his capacity for physical effort is greater, his pulse rate is 78, rising to 134 on physical exertion, and falling to 60 a minute thereafter. In this case the improvement may be ascribed to digitalis fully as well as to quinidine. In one case (Case X.) the auricular fibrillation was converted into flutter, at a rate of 292 per minute; the individual was neither better nor worse; the normal rhythm was never restored; the fibrillation recurred and persisted in spite of the continued administration of quinidine. In the remaining 8 cases the fibrillation persisted unchecked and the patients experienced no benefit from the drug. Quinidine is therefore no certain cure for fibrillation. It may be given a trial in suitable cases, namely, in patients who have fibrillation without serious cardiac failure and who are not dropsical or cyanotic. In some of these selected cases quinidine may, by bringing fibrillation to an end and thus restoring the normal rhythm, relieve the patient of his most distressing symptoms, but the drug will not cure him of the disease of which the fibrillation is but a manifestation. It is not sufficiently recognised that auricular fibrillation occurs essentially in cases of chronic myocarditis. In the majority of cases this is secondary to disease of the coronary arteries; in one-third of the cases the myocarditis is of rheumatic origin and develops in the late stages of mitral valvular disease. Histological examination of the auricular walls of these cases often reveals not only a subacute myocarditis, but a considerable degree of interstitial fibrosis. In the auricular fibrillation associated with exophthalmic goitre, hyaline degeneration of the auricular muscle fibres may be found. Under the influence of quinidine the abnormal functional state of the auricular muscle may temporarily improve, but we have as yet no evidence to show that the drug exerts any effect on inflammatory and degenerative processes within the auricular wall.

Quinidine Sulphate in Auricular Fibrillation

Synopsis of Cases.

Case I.—Mrs M'I., aged 45. Rheumatic fever in girlhood. Well until birth of last child in 1915. Admitted to Deaconess Hospital, 5th October 1921 complaining of shortness of breath and cough; mitral stenosis and incompetence, persistent auricular fibrillation; no dropsy; Wassermann reaction negative.

Quinidine sulphate, commenced on 10th October, was given in two doses of 0.2 gram, twelve doses of 0.4 gram, total, 5.2 grams. in seven days. Two days after the quinidine was discontinued she had a paroxysmal attack of dyspnœa and coughing, lasting for one hour. *Result:* Fibrillation persisted.

Case II.—J. D., tailor, aged 63. No history of rheumatic fever. Breathless for five years; slight palpitation. Admitted to Deaconess Hospital on 17th October 1921, with mitral incompetence, dropsy, orthopnœa; Wassermann reaction strongly positive. Urea concentration test 2.9 per cent. at end of second hour. Improved by rest in bed and digitalis.

Quinidine sulphate commenced on 15th November. After two initial doses of 0.2 gram, he was given 0.4 gram night and morning for seven days, and 0.4 gram once daily for fourteen days; total, 11.6 grams in twenty-two days. *Result:* Fibrillation persisted.

Case III.—Mrs A. B., aged 53. Admitted to Ward 3 of the Royal Infirmary on 10th December 1921, with persistent auricular fibrillation; heart slightly enlarged, the first sound at apex impure; no dropsy. Persistent trace of albumin. Melancholia.

Quinidine sulphate commenced on 11th December. After three initial doses of 0.2 gram, she was given 0.4 gram twice daily for nine days, 0.4 gram thrice daily for one day, 0.4 gram six hourly for two days, and 0.4 gram once. Total, 12.6 grams in fifteen days. *Result:* Fibrillation persisted.

Case IV.—P. S., cabdriver, aged 56. Syphilitic infection at age of 21. No history of rheumatism. In January 1920 was off work for six weeks because of breathlessness and palpitation. Admitted for the fifth time to the Royal Infirmary, under the care of Professor Gulland, on 27th December, 1921. On former occasions relieved by rest and digitalis. On re-admission, cyanosed, slight dropsy; Wassermann reaction strongly positive. No valvular disease; persistent auricular fibrillation, ventricular rate 60 to 96.

Quinidine sulphate commenced on 30th December. After an initial dose of 0.2 gram, he was given 0.4 gram once daily for two days, 0.4 gram night and morning for two days and 0.4 gram thrice daily for three days. Total, 6.2 grams in eight days. *Result:* Fibrillation persisted.

Case V.—A. M. aged 36. Malaria in July 1916. Persistent auricular fibrillation since February 1918. Exophthalmic goitre since May 1920. Admitted to Craigleith Hospital on 5th January 1922. Consolidation of apex of left lung; Wassermann reaction negative.

Quinidine sulphate commenced on 10th January. After an initial dose of 0.2 gram he was given 0.4 gram thrice daily for six days, and 0.4 gram six hourly for eight days. Total, 20.2 grams in fifteen days. *Result:* Fibrillation persisted.

Case VI.—W. T., glassblower, aged 35. November 1915, gunshot wound of left chest, no history of rheumatism. December 1919, dyspnœa and exhaustion. January 1920, cerebral embolism causing left hemiplegia. November 1920, mitral stenosis, auricular fibrillation, ventricular rate 156; subsequently persistent fibrillation. Admitted to Craigleith Hospital, 26th January 1922. Wassermann reaction negative.

Quinidine sulphate commenced on 28th January. After initial doses of 0.2 gram twice daily for two days, he was given 0.4 gram three times on the third day and 0.4 gram twice daily from the fourth to seventh day. During the period from the fourth to seventh day the rhythm was normal. Thereafter persistent fibrillation, despite the continued administration of quinidine for twelve weeks, the minimum daily dose during this period being 0.6 gram, and the maximum daily dose, which was continued for one week, being 1.6 gram. Total, 70.2 grams in three months. *Result:* Restoration of normal rhythm for four days, followed by persistent fibrillation.

Case VII.—Mrs C. M., aged 45. Probable onset of auricular fibrillation, March 1920. Admitted to Deaconess Hospital on 4th February 1922. Mitral incompetence with chronic venous congestion of viscera, persistent auricular fibrillation.

Quinidine sulphate commenced on 9th February, given in doses of 5 gr. (.324 gram) thrice daily for twenty days. Total, 19.4 grams in twenty days. *Result:* Fibrillation persisted.

Case VIII.—G. W., labourer, aged 36. History of pneumonia; no history of rheumatic fever. Mitral stenosis and persistent auricular fibrillation since December 1919. Admitted to Craigleith Hospital, 30th January 1922. No dropsy; Wassermann reaction negative.

Quinidine sulphate commenced 18th January. Given 0.2 gram twice daily for four days, 0.4 gram twice daily for two days, 0.4 gram thrice daily for nine days. Total, 10.4 grams in fifteen days. On the thirteenth day the normal rhythm was restored, with extrasystolic ventricular tachycardia at rate of 146 per minute. Quinidine sulphate discontinued; four days later fibrillation recurred. On 9th March commenced digitalis tincture, 10 minims thrice daily; on 18th

March normal rhythm at rate of 64 per minute. From 1st April to 3rd April quinidine sulphate 0.4 gram given thrice daily, and from 4th to 30th April 0.2 gram twice daily; also given digitalis tincture in doses of 10 to 15 minims, thrice daily. Since 18th March normal rhythm with occasional auricular extrasystoles. *Result:* Success.

Case IX.—A. M., tramcar driver, aged 58. Pernicious anæmia of several years' duration. Admitted to the Royal Infirmary, under the care of Professor Gulland, 21st January 1922, complaining of weakness, palpitation, breathlessness, cough, and indigestion, mitral incompetence, persistent auricular fibrillation. Wassermann reaction negative. Red cells, 3,730,000; leucocytes 5800; hæmoglobin 75 per cent.

Quinidine sulphate commenced on 20th February. After two initial doses of 0.2 gram, given 0.4 gram on the third day, 0.6 gram on the fourth day, 1.2 gram from the fifth to the tenth day, inclusive. On the ninth day impure flutter at an approximate rate of 250 per minute, ventricular rate of 72 to 88 per minute. On the tenth day normal rhythm, at rate of 71 per minute. On the eleventh day quinidine sulphate given in doses of 0.4 gram twice daily; thereafter ceased. Total, 9.4 grams in eleven days. On the seventeenth day, normal rhythm still maintained at rate of 59 per minute. Discharged from hospital on the nineteenth day. *Result:* Success.

Case X.—J. M'C., miner, aged 47. Influenza and pleurisy in 1917. No history of rheumatism or syphilis. On 4th August 1921 while at work, sudden onset of pain in epigastrium, left side of chest and left shoulder; also of dyspnœa and palpitation. These symptoms persisted. Admitted to the Royal Infirmary under the care of Professor Gulland on 1st March 1922. Arterio-sclerosis, persistent auricular fibrillation, slight cyanosis, Wassermann reaction twice negative, no valvular disease, no dropsy.

Quinidine sulphate begun on 2nd March. After an initial dose of 0.2 gram the dose was increased from 0.2 gram thrice daily to 0.4 gram four hourly. On the seventh day, after taking 6 grams, there was impure flutter at a rate of 292 per minute. Thereafter fibrillation persisted for three weeks, despite the continued administration of quinidine in doses of from 0.4 to 0.8 gram daily. Total, 50.4 grams in fifty-nine days. *Result:* Fibrillation persisted.

Case XI.—Mrs H., aged 50. Intermittent rheumatism from age 19 to 43. Intermittent dropsy for four and a half years. Admitted to Deaconess Hospital, 30th May 1921. Mitral incompetence, persistent auricular fibrillation, dropsy. Wassermann negative. Gradual improvement by means of rest and digitalis.

Quinidine sulphate begun on 1st March 1922. Given in doses of

0.2 gram twice daily. This was discontinued after three days because of nausea and breathlessness. *Result:* Failure.

Case XII.—T. J. W., aged 40. December 1917, suffered from subacute rheumatism and dilatation of the heart; pronounced and persistent irregularity of pulse first observed in August 1918. Admitted to Craigleith Hospital on 2nd March 1922. Apex beat in sixth interspace 4½ inches from mesial line; auricular fibrillation; ventricular rate 115. No dropsy; Wassermann reaction negative; urine normal.

Quinidine sulphate given in doses of 0.2 gram thrice daily for three days; after two days' interval, given in doses of 0.4 gram thrice daily for four days, then 0.4 gram four hourly for two days. Fibrillation persisted. A second course of quinidine in doses of 0.4 gram six-hourly, making a total of 9.6 grams in nine days, likewise failed. *Result:* Failure.

Discussion.

Dr Rainy congratulated Dr Ritchie on his most valuable contribution. He recalled the observations of continental pharmacologists on the action of cinchona alkaloids upon the heart dating back to the last decade of the nineteenth century, whilst more recent work had given an increasingly accurate and precise explanation of the mechanism involved. He regarded Dr Ritchie's paper as marking a distinct step in this progress, and as particularly valuable in helping to define the limits that exist to the usefulness of the drug and the precautions to be observed in its employment.

Dr Murray Lyon gave a few details of some cases of auricular fibrillation which he had treated with quinidine. He said that there was no doubt that quinidine slowed the auricular rate even when a normal rhythm was not restored. Quinidine also increased the ventricular rate, and if given alone might do harm to the patient. For this reason the patient should be prepared for treatment by giving him a preliminary course of digitalis. This drug should also be continued during the administration of quinidine. In the present state of our knowledge it was difficult to follow clinically the action of quinidine. The pulse might become regular under digitalis alone, while the auricles continued to fibrillate, or under quinidine a regular ventricular rhythm might occur although the auricles were beating two, three, or four times as fast. For this reason he emphasised that quinidine could only be successfully employed by those who were able to follow the changes in the auricles by means of the electrocardiograph or the polygraph.

THE PLASTIC SURGERY OF THE NOSE.*

By DOUGLAS GUTHRIE, M.D., F.R.C.S.

By way of introduction to a Lantern Demonstration, Dr Guthrie showed three patients who had undergone operations for nasal disfigurement.

I.—C. F., aged 16, suffered from lupus fourteen years ago, when the disease destroyed the bridge, columella and tip of the nose. These parts have now been restored.

II.—L. L., aged 20 (deformity from injury) was shown before this Society two years ago, and has now appeared again, to illustrate the permanence of the result secured by transplantation of cartilage.

III.—E. M., whose nose was distorted by congenital syphilis, illustrates how a good result might be secured even when the vitality of the tissues was low.

The various operative procedures were then demonstrated with the aid of lantern slides. That the reconstruction of a nose was no modern invention of surgery was proved by the work of Tagliacozzi who, as early as 1570, had perfected the method of transferring a flap from the arm to form a new nose—the so-called Italian method. This operation was still in vogue. The sacrifice of a finger to gain a nose was also sometimes practised, but was hardly justifiable. Those operations had now been largely superseded by the use of local flaps from the forehead, the Indian method of Keegan and other I.M.S. surgeons, and improved by the recent work of Major Gillies.

Photographs were exhibited, showing in its various stages a case of nasal reconstruction in a man whose nose had been destroyed by an electrical accident. It was essential to provide a lining for all flaps, so as to avoid subsequent shrinkage. Support was secured by imbedding strips of cartilage in the tissue destined to form the flap. The reparative power of Nature was great, and considerable time should be allowed between operations, when proceding by stages. At times it was advantageous to employ a long flap from the forehead or neck, the terminal portion being used to rebuild the defect, while the proximal portion or pedicle was folded so as to form a tube and thus conserve the blood supply. At a later date the pedicle was divided and returned to its original bed. Examples of the tube flap were shown.

* Read 3rd May 1922.

Gross defects, which demanded treatment by complete rhinoplasty, were seen much less frequently than minor deformities, which involved only a part of the nose. The first patient on view this evening underwent a series of minor operations. The bridge was first restored by a graft of costal cartilage. Then the tip was reconstructed by two small lateral flaps, and finally a columella was secured by a broad flap from the skin between nose and lip.

Photographs of a second case of lupus were shown. The bridge of the nose had been rebuilt by means of costal cartilage, as described before this Society last year (*Edin. Med. Journ.*, Dec. 1921). The slide was interesting, as one might note how the mental outlook of the patient had improved since the disfigurement had been corrected.

A syphilitic deformity, involving loss of bridge, septum and columella, presented a difficult problem owing to the cicatricial contraction which was often considerable. A case of this nature was illustrated, also a case of loss of the ala nasi from the bite of a horse, after treatment by the Italian method of rhinoplasty. Harelip deformities of the ala nasi were best corrected by inward transplantation of the ala, followed by the implantation into the cheek of a piece of cartilage from the nasal septum. This had the effect of supporting the ala in its corrected position.

PRIVATE BUSINESS.

Meeting — 3rd May 1922.

The following were unanimously elected Corresponding Members of the Society.—Eugenio Tanzi, Professor of Psychiatry in the Royal Institute of Florence; Guiseppe Bastianelli, Polyclinic Hospital, Rome; Karl Anders Petrén, Professor of Medicine in the University of Lund; Pierre Marie, Membre de l'academie de médicine, Paris, Professeur de Clinique des Maladies nerveuses à la Faculté de Paris; Harvey Cushing, Professor of Surgery, Boston, Mass., U.S.A.; George Washington Crile, Professor of Surgery, Western Reserve University, Cleveland, U.S.A.; Hermann Michael Biggs, M.D., Commissioner State Department of Health, New York, U.S.A.; Alex. Blackhall-Morison, M.D., F.R.C.P. Edin. & Lond., Consulting Physician, Great Northern Central Hospital, London; Sir Frederick Walker Mott, K.B.E., LL.D., M.D., F.R.C.P., Lond., F.R.S., Pathologist to the London County Asylums; Alex. Primrose, C.B., M.B., C.M. Edin., Professor of Clinical Surgery in the University of Toronto.

James Alston, M.B., Ch.B., was elected a Member of the Society.

AN ALTERNATIVE METHOD OF ADMINISTERING VACCINES.*

By DAVID LEES, D.S.O., M.B., F.R.C.S., Edinburgh.

In disease, the acquisition of immunity may be the result of natural processes. This is often slow in its production, and in many cases of infectious disease attempts are made to induce artificially the production of a more rapid immunity, with a view to cutting short the disease and hastening the patient's recovery from it.

Two methods are available (1) passive immunisation, in which serum produced in an immune animal and containing the products of active immunisation is introduced into the infected person; and (2) active immunisation in which killed organisms are injected to stimulate in the infected person the production of immune substances. In the latter, the duration of the resulting immunity is likely to be considerably greater than if acquired by passive immunisation, but the protected condition is often preceded by a period of increased sensitiveness or negative phase.

This period is more marked if the dose of bacterial vaccine is a large one and if the vaccine *per se* is of a highly toxic nature. Many attempts have been made to overcome toxicity in the therapeutic use of vaccines. In 1892, Lorenz recommended a method of sero-vaccination in swine erysipelas. A more important advance in this respect was the introduction in 1902 by Besredka of sensitised vaccines, in which the bacillary bodies were first killed by heat and then exposed to their specific immune serum, the excess of which was removed by centrifugally washing the sensitised bacteria.

He claimed that this avoided or at least shortened the negative phase, rendered the vaccine non-toxic and produced a lasting immunity. His work was confirmed by Levy and Ham in 1909 in the use of streptococcal vaccine in puerperal fever, by Calmette and Guerin in 1910, in the use of tuberculin, and by Metchnikoff in 1911 in the use of typhoid vaccine.

In 1901, Pfeiffer working with typhoid and cholera bacilli, stated that sensitised vaccines did not produce bacteriolytic bodies and had lost their immunising properties, and Rowland,

* Read 3rd May, 1922.

in 1912, reported that he found them to be as toxic as the non-sensitised vaccine and no more effective therapeutically.

In 1916, Kakehi found that the negative phase set up by them was only slightly lessened, while the production of antibody was much less with the sensitised than with the ordinary vaccine. Efforts in other directions have been made to produce a vaccine which would produce a rapid immunity response and yet avoid the negative phase with its local, focal, and general reactions. Autolysation, digestion, and detoxication of the organisms are some of the methods which have been suggested. In the latter process devised by Thomson in 1918, the toxins were removed by washing with 0·5 per cent. sodium acid phosphate and 0·5 per cent. phenol. Since then he has improved the technique of this process and claimed that without altering the specific antigenic properties of a vaccine, much larger doses could be administered and more rapid and lasting immunity produced by detoxicated vaccines, than by other vaccines. In the treatment of gonococcal and genito-urinary infections this claim is substantiated and is supported by Harrison, Mills, MacDonagh and many other workers in urogenital work.

While there is no doubt that detoxication reduces the toxicity and to a great extent eliminates the period of hypersensitiveness or negative phase, in which clinical signs are exacerbated, it does not completely eliminate it, especially in hyper-acute conditions, when it is given in sufficient dosage to produce therapeutic immunisation.

Vaccine Therapy in Clinical Work.—In acute infections the general tread of clinical opinion is that there is already sufficient antigen present in the tissues to stimulate the formation of antibody, and that by introducing additional antigen in the shape of a vaccine, the immune producing tissues are overtaxed. This is to some extent the cause of the temperature reaction of the patient and the subsequent hypersensitive phase when clinical signs of the infection are exacerbated.

It is generally agreed, however, that in subacute and chronic infections where the infecting antigen has become less virulent and the immunity-producing tissues have, as it were, established a balance against the infecting organism, the exhibition of a therapeutic dose of vaccine does not so readily produce toxic symptoms or gross reactions, and acts rather as a stimulus to the existing antigen.

While these general remarks are applicable to many types of infection, they are not in my experience applicable to gonococcal infection of the lower genito-urinary tract, or of any other part of the body. Acute gonococcal infections no less than subacute and chronic conditions react well to the administration of a specific vaccine. The difficulty is to know which case will tolerate potent dosage, and the therapeutic immunisation must be carefully guided by the local, focal, and general reaction. No arbitrary scheme of dosage can be laid down, and the locality of the infection is often an important factor in the production of the reaction and of the negative phase which succeeds the administration of a vaccine. Thus a case of prostatitis or of acute salpingitis will not tolerate the same dosage as a case of acute anterior urethritis or acute conjunctivitis will.

In a certain percentage of cases gross reactions are set up, and no matter how specific the vaccine or how potent antigenically, or how carefully given, it does not give rise to an immediate immunity response. The patient in such cases shows mild anaphylactic symptoms, such as rigors, malaise, headache, sickness, etc. A negative phase is induced, and the patient's resistance to the infection is lowered and cure is appreciably retarded. This occurs in acute prostatic infections in the male and in acute tubal conditions in the female, more so than in any other type of genito-urinary infection. Clinically at least, during the negative phase, the patient appears to be in a condition exactly the opposite of immunity, *i.e.*, in a condition of hypersusceptibility to the infecting agent. With a view to lessening this phase of hypersusceptibility and to avoid reactions subsequent to the administration of a potent dose of a vaccine, Besredka's method of desensitising animals to sera and other proteins appeared to me a method which might be adopted in the therapeutic use of vaccines in acute and hyperacute conditions, where the patient was already, as it were, sensitised to his existing infection.

Use of Desensitisation in Preventive and other Inoculations.—This method of producing anti-anaphylaxis was used effectively by Besredka and Cruveilhier in immunising female goats against the gonococcus and the diphtheria bacillus, the first dose given being ten times weaker than the subsequent massive dose. Dopter and Briot adopted it in immunising horses against the meningo-coccus, and Biuca in the protec-

tion of horses intended for the preparation of anti-streptococcal and anti-diphtheritic serum. Where previously three out of every five horses succumbed to anaphylactic symptoms in eight to ten minutes, no deaths occurred when this method was adopted.

Application of this Method in the Administration of Vaccines.—In the therapeutic use of vaccines in potent and almost heroic doses, this method has now been used by me in over 100 cases of gonococcal infection and its complications. The reaction following the second or therapeutic dose of bacteria has been in every case relatively weak. However massive the dose, the temperature next day has been almost always normal, and the general condition of the patient has invariably been improved when desensitisation was previously practised.

The organisms to which the patients have been desensitised have varied according as the infecting agent has been the gonococcus, staphylococcus, *b. coli*, diphtheroid bacillus, pneumococcus, etc. In every case specific therapy was applied, the desensitising agent and the subsequent therapeutic vaccine containing only such organisms as were isolated by smear or culture. Stock vaccines, autogenous vaccines and detoxicated vaccines were used either separately or in combination.

Two methods were employed in the desensitising process, either (*a*) the intramuscular or subcutaneous route, or (*b*) the intravenous route.

In the former, three to four hours are allowed to elapse between the desensitising and the therapeutic dose; in the latter, ten to twenty minutes is quite sufficient time for desensitisation to occur. The intraspinal method which requires one to two hours has not been practised.

The most rapid and the most certain method is the intravenous route, the phenomenon occurring almost immediately. The technique adopted has been as follows: After isolating the infecting organism, a dose equivalent roughly in the case of a polyvalent stock vaccine or autogenous vaccine to $\frac{1}{100}$ to $\frac{1}{1000}$ of the ordinary average dose has been administered intramuscularly or intravenously. Two hours subsequently in the former and fifteen minutes in the latter, maximal therapeutic doses have been given intramuscularly, in the case of stock vaccines, up to 1000 million, in autogenous up to 750 million, and in the case of detoxicated vaccines as high as 30,000 million germs.

Combinations of these vaccines have also been given, *e.g.*,

detoxicated gonococcal vaccine in combination with an autogenous vaccine containing diphtheroid bacilli and *bacillus coli*. All types of infection have been treated, but mainly those of the lower genito-urinary tract. (Urethritis and its complications, such as arthritis, epididymitis, etc., in the male, and acute, subacute and chronic infections in the female.) In none of them has there been anything beyond a slight local reaction to the second massive dose, focal reaction is usually absent, and the general reaction rarely exceeds 1° of temperature. The febrile period of the disease if present is rapidly reduced, the bad general condition seen in many of the prostatic and arthritic complications which ordinarily persist for weeks is cleared up and the lassitude, malaise, etc., which often succeeds the initial dose of a potent vaccine is completely absent.

Case Reports Illustrating Results Obtained.

Case I.—R. H., aged 39, male. Exposed to infection 22nd July 1921, reported on 26th July with mucopurulent discharge and burning sensation on passing urine. Urines were (1) turbid; (2) clear; (3) clear; pointing to an infection of anterior urethra only. There was no frequency. Urethral smear showed gonococci both extra and intracellular and pus cells. Temperature 99° F.

Progress and Treatment, 26.7.21.—Desensitised intravenously with polyvalent detoxicated gonococcal vaccine, containing 250 organisms. Therapeutic dose fifteen minutes later of 20,000 million gonococci. Anterior urethra was washed with solution of 1/10,000 pot. permang. Temperature 99.1°. No local or focal reaction.

28.7.21.—Discharge mucoid and smear of it showed only epithelium and scanty pus cells. No gonococci were demonstrated. Urines were clear by three glass test. Anterior urethra washed out with permanganate solution 1/10,000. Temperature 98° F. No local or focal reactions.

29.7.21.—No discharge and no smear available. Urines clear. Microscopic examination of centrifuged urine deposit showed only a few epithelial cells. Anterior urethra washed out with 1/10,000 pot. permang. Temperature 98.2° F.

29.7.21.—No discharge and no smear available. Urines clear. Microscopic examination of centrifuged urine deposit showed only a few epithelial cells. Anterior urethra washed out with 1/10,000 pot. permang. Temperature 98.2° F.

30.7.21.—No clinical or bacteriological signs of disease. Treatment stopped. Infection aborted. This patient was observed once weekly for one month and once monthly for the succeeding five months and

has shown up to now no clinical or bacteriological signs of gonorrhœa. He has in addition been subjected to all the tests mentioned later.

Case II.—A. R., aged 27, male. Exposed to infection 28.4.21. Urethral discharge appeared 2.5.21 with pain and slight frequency. Reported for treatment 9.5.21 (seven days).

9.5.21.—On admission discharge was profuse and purulent and contained pus cells, gonococci and staphylococci; urines by two glass test were turbid and contained pus threads. Urethra was washed out with pot. permang. 1/8000 and this was repeated daily for first eight days. Desensitised at 10.30 A.M., intramuscularly and therapeutic dose of detoxicated gonococcal and staphylococcal vaccine, 20,000 million given at 12.30 P.M. At 7 P.M. discharge was very much decreased and pain had disappeared.

10.5.21.—Very slight mucopurulent bead of discharge and no sign of either local, focal, or general reaction.

11.5.21.—No apparent discharge and urines clear, but still containing a few threads.

Although this patient showed only no clinical signs of urethritis apart from a very slight mucoid discharge on milking the urethra and his urines remained clear, gonococci were demonstrated in the mucoid material from his urethra for twenty-three days. Active immunisation was continued at intervals of five to seven days during this time. Subsequent to this date, 7.6.21, no clinical or bacteriological signs of urethritis have been observed and the patient is still under observation and attending for syphilitic treatment.

Case III.—Female, aged 24, married; seen 12.12.21 complaining of acute pain in suprapubic region, frequency and urgency of micturition every half hour and pain on passing water. Urine was acid and contained on examination *bacillus coli*, the result being later confirmed by pure culture. There were no clinical or bacteriological signs of gonococcal infection and no reason to suspect it. Temperature 100.2° F.; pulse 110. Antifebrin gr. iv and atropine gr. 1/75th was given in suppository after a hot sitz bath, and the same evening the patient was desensitised intravenously with a detoxicated polyvalent vaccine of *bacillus coli*, and twenty minutes later a therapeutic dose of 5000 million was administered.

13.12.21.—Pain, frequency and urgency had disappeared. *Bacillus coli* still present in urine. There was a local but no focal reaction and temperature was normal.

14.12.21.—Patient felt well and was able to be up. Temperature normal. *Bacillus coli* not demonstratable in urine.

This patient is still under observation and has had no recurrence of symptoms, and the urine examined from time to time has not shown *bacillus coli* on culture.

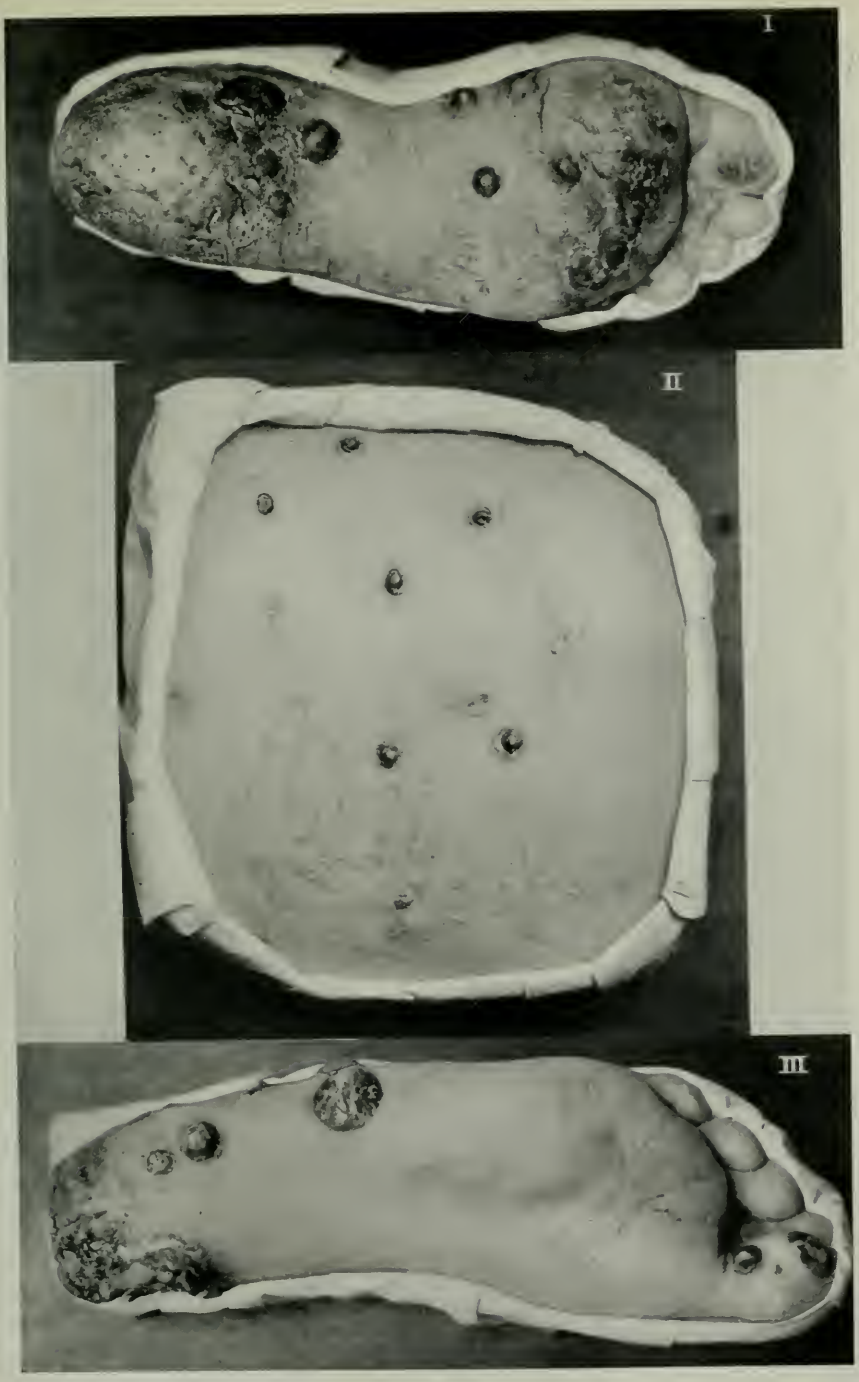


FIG. I.—Keratodermia Blennorrhagia on Sole of Foot (page 125) treated by desensitisation method. (*Cf.* Fig. IV.)

FIG. II.—Keratodermia Blennorrhagia on Back treated by desensitisation method. (*Cf.* Fig. V.)

FIG. III.—Keratodermia Blennorrhagia on Sole of Foot not treated by desensitisation method.

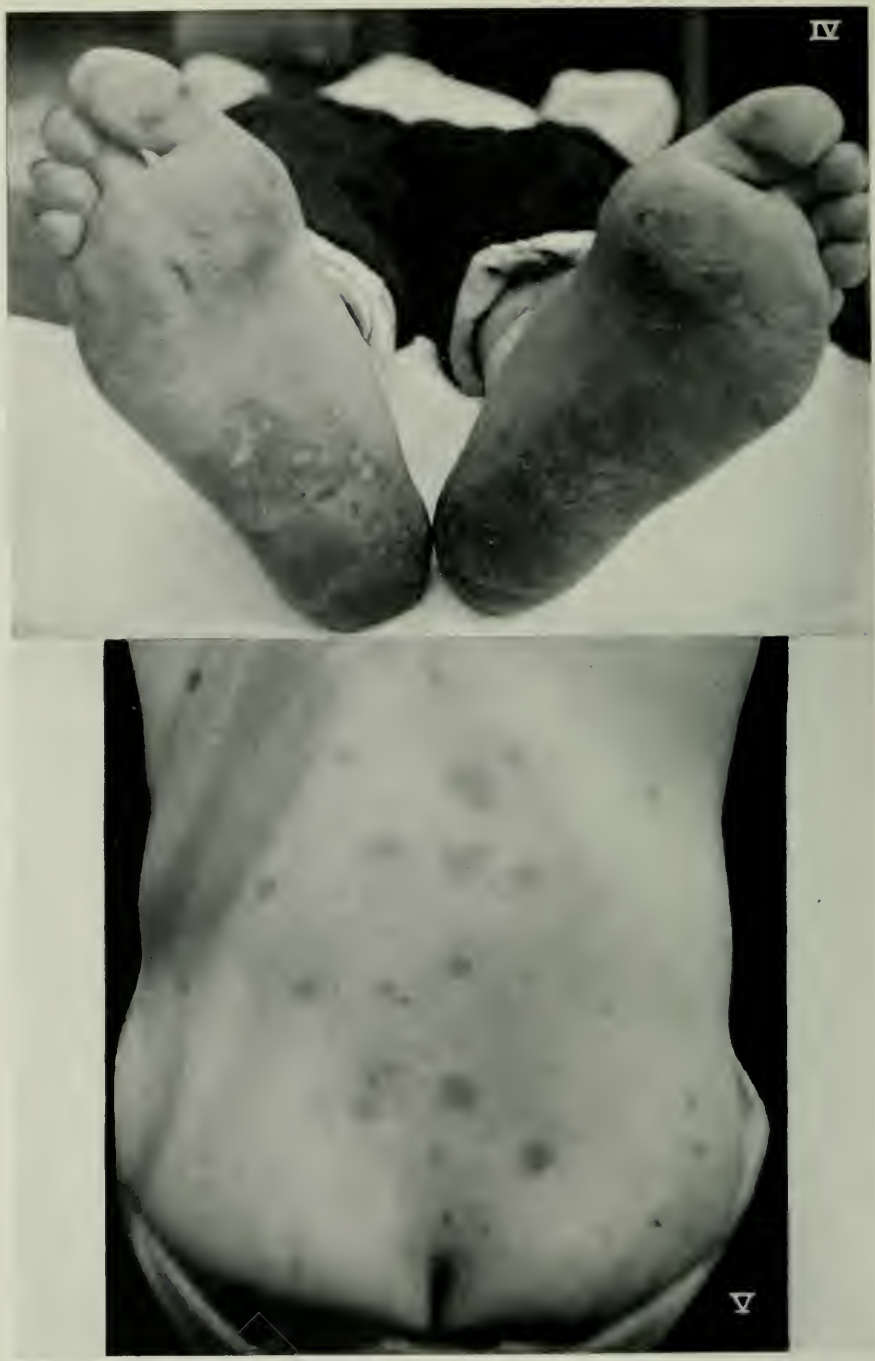


FIG. IV.—Condition of Feet in Fig. I. Eighteen days after desensitisation method of treatment commenced. (*Cf.* Fig. I.)

FIG. V.—Condition of Back in Fig. II. Eighteen days after desensitisation method commenced. (*Cf.* Fig. II.)

Case IV.—M. E., male, aged 26, with history of gonorrhœa in 1915 and a fresh infection in September 1921. The condition with ordinary treatment became subacute and when first seen on 24.11.21 the condition had flared up and he had an acute attack of epididymitis, a prostatic abscess and vesiculitis. The prostatic abscess had burst into urethra.

24.11.21.—Condition on admission: Discharge purulent. Urines (1) turbid and containing gross threads; (2) turbid; (3) turbid. Smear showed pus cells and gonococci.

Progress and Treatment, 24.11.21.—Daily lavage of urethra with albargin 1/5000 for first ten days. Desensitised intravenously with detoxicated gonococcal vaccine and therapeutic dose given ten minutes later of 25,000 million gonococci. Temperature 99° F.

25.11.21.—Discharge was gleety only. Urines were (1) turbid and threads; (2) clear; (3) clear. Prostatic urine was turbid. There was no focal reaction, a slight local one and temperature 100° F.

28.11.21.—Discharge had disappeared and first urine had almost lost its turbidity. Temperature normal. Gentle prostatic massage commenced. This patient was seen twice weekly for prostatic massage and instrumental treatment subsequently, and at no time was any discharge apparent, and the enlarged prostate, vesicles, and epididymis became normal by 27.12.21. He was seen as recently as 7.4.22, and has had no signs or symptoms of disease, and complement fixation test is now "negative."

Case V.—E. S. M., male, aged 30, who had been treated for six months for chronic urethritis.

3.8.21.—Seen with acute epididymitis of three days' duration, the result of sexual excess. There was a very slight mucoid to mucopurulent discharge which contained pus cells and *bacillus coli* and diphtheroid bacilli on culture. Urines were turbid in three glass test.

5.8.21.—Desensitised to autogenous *bacillus coli* and diphtheroid bacilli, and fifteen minutes subsequently therapeutic dose of detoxicated *bacillus coli* and diphtheroids, plus autogenous vaccine—15,000 million diph. detox., 1500 million *b. coli* detox., and 500 million autogenous.

7.8.21.—Pain and swelling in epididymis had disappeared and on 8.8.21 urines were clear and free from pus. He was able to ride on horseback without discomfort. Kept under observation till 12.11.21 and had no return of symptoms although partaking freely of alcohol and indulging in sexual coitus.

Case VI.—A. L., male, aged 33, suffering from neurasthenia was advised by his medical attendant to have a course of diphtheroid vaccine, isolated from his fæces, but could not tolerate as minute doses as 2 to 3 million of the organism, owing to the gross general reaction set up. The same organism was isolated from his prostatic

secretion and an autogenous vaccine prepared. After desensitisation he was able to tolerate a dose of 500 million, and this was gradually increased to 1000 million,' 24 doses in all being given. Coincidently his general condition of neurasthenia showed progressive improvement.

Case VII.—I. G., male, aged 34. Gonorrhœa fifteen years previously and subsequent reinfection January 1921, for which he was treated by protargol injections by his doctor. Seen on 7.5.21. Condition: Discharge purulent; urines (1) turbid; (2) turbid; (3) turbid. Prostate and vesicles were both acutely involved. Pain on passing water, frequency and urgency were present. Smear showed pus and gonococci. Temperature 98.6° F.

Treatment and Progress, 7.5.21.—Desensitised and subsequent dose of detoxicated gonococcal vaccine, 20,000 million given intramuscularly. No focal or general reaction but fairly severe local reaction for ten hours. Intravesical lavage with pot. permang. 1/8000 and administration of an alkaline diuretic.

9.5.21.—Discharge—mucoid only and urines almost clear. No urgency or frequency.

11.5.21.—No apparent clinical signs of disease and urine only showing threads. No gonococci obtainable from secretions. Prostatic massage commenced.

15.5.21.—Therapeutic dose repeated of 20,000 million gonococcal vaccine. No sign of disease.

This patient was kept under observation and subjected to instrumental treatment for infiltration of his urethra and all tests of cure were tried during the next three months, without finding any focus of disease. He continued well when last seen in January 1922 and complement fixation test was then "negative."

Case VIII.—O. W., aged 36, male. Reported 1.11.21 with subacute urethritis and prostatitis and vesiculitis. He had a mucopurulent discharge and his urines were turbid. Urethral infection had been present for six months and culture of prostatic secretion showed gonococci, staphylococci, and pneumococci. An autogenous vaccine was prepared, and after desensitising he was given on 6.11.21 ½ c.c. of his autogenous vaccine containing 500 million g. c., 500 million staphylococci, and 500 million pneumococci. There was no reaction—only a slight feeling of malaise and pain over the precordia for six to eight hours subsequently. By the third day the discharge had disappeared and the urines were clear but still contained filaments. Weekly increasing massive doses of vaccine were continued until a dose of 2000 million organisms was reached. This patient was kept under observation until 31.1.22. His urethra was dilated to size 36 French scale, and he was subjected successfully to all known tests of cure. He reported at the end of March that he was still well.

General Remarks on Cases.—These are a few of the cases in which this method of producing active immunity has been practised. In quite a percentage of cases the acute clinical signs of disease are markedly ameliorated in twenty-four to forty-eight hours.

Not infrequently the patient who is treated by this method for an early acute urethritis returns the following day with no apparent signs or symptoms of disease and the infection has been aborted. This condition of apparent immunity remains in others for, roughly, five to six days, when there may be a slight return of symptoms, but these disappear as quickly on the administration of another therapeutic dose of vaccine and a third dose is often sufficient to clear up the infective process.

The same phenomena occur in many of the acute complications of urethritis. The pain and frequency in acute prostatic, vesicular, and epididymis cases is very appreciably lessened and the joint pains in arthritis are alleviated.

A case of arthritis who had been confined to bed on the medical side of the hospital for three weeks and to whom salicylates had been given without relief for multiple acute arthritis, involving the left shoulder and hip, both knees and one ankle-joint, was able to walk about the ward forty-eight hours after this method of therapy, and at the end of ten days to attend as an out-patient. A case of gross polyarthritis with an associated vesiculitis and in addition hyperkeratosis blennorrhagia, a condition which usually takes months to clear up, was able to leave the ward and attend as an out-patient in eighteen days (Figs. I. II. IV. V.). A female patient with a persistent subacute endocervicitis and subacute salpingo-ovaritis, in whom gross vaginal and cervical discharge had persisted for months, in spite of antiseptic treatment, was free from all signs of vaginal or cervical discharge twenty-four hours later as a result of desensitisation and subsequent massive dosage of autogenous vaccine.

While some of the results are spectacular in their rapidity, there are others in which no effect is produced on the course of the disease apart from the preliminary temporary cessation of the gross symptoms. The majority of these latter are out-patients who are not under such close observation and who are carrying on their daily work, which does not allow of the best conditions for combating the infective process, while in other

cases the essential dietetic and local treatment has not been possible on account of the necessity for secrecy.

In-patient cases in general do better than out-patients.

In very few of the cases have any complications supervened which could be attributed to this method of treatment. In a number of cases of established urethritis, gonococci can be demonstrated in the very slight mucoid or gleety discharge for a considerable time after disappearance of acute signs of disease, and the patient, unless he remains under observation and treatment, may become a carrier, or misled by the apparent cure, may later have a recurrence of his symptoms.

Standard of Cure Adopted.—In all the successful cases a rigid standard of cure has been adopted. Absence of clinical signs for long periods after cessation of treatment, the passage of bougies, dilatation and suction of the urethra, prostatic massage, provocative vaccines and subsequent repeated bacteriological and cultural examination of the urine and of smears, have all been employed to find any latent focus of infection. Every case has been examined by urethroscope, and in a large number the blood has been examined by complement fixation test.

Cases most Suitable for this Method of Treatment.—When the results of 100 cases so treated are examined by these standards, certain types of case show better results than others. Early acute infections of the urethral tract give the most rapid and consistently good results, and in the greater number of cases seen within twenty-four hours after the appearance of symptoms the disease can be successfully aborted.

Acute exacerbations supervening on a chronic or latent process also react well, and are appreciably lessened in their severity and in their duration. In established acute and subacute conditions, the gross clinical signs and symptoms are ameliorated, and the patients can carry on their daily occupation with more comfort and with less likelihood of their infection being discovered. Such cases, on the other hand, if they do not continue under treatment, are, I think, extremely liable to become carriers of disease.

General Conclusions.—I am not able to offer any explanation of the mechanism by which this process acts, unless it be that the desensitising dose produces what Besredka has called a condition of antianaphylaxis to the infecting antigen present in the body. It will thus temporarily neutralise or cut out the existing toxæmia set up by the infection, and allow the body

tissues, fluids, and blood, free play to steadily produce antibody to the existing infection on the stimulus of a potent dose of vaccine. I think we may be certain that it has nothing in common with the recognised processes of active immunisation, *i.e.*, with the production of agglutinins, bacteriolysins, etc., against bacteria and their toxins, as these substances are not usually demonstrable in the blood serum in gonorrhœa until after a lapse of seven or eight days at least. The only feature the two conditions have in common is their specificity.

It is just possible as suggested by Danysz that during the incubation period of an infectious disease, the host passes through a period of sensitisation to the infecting organism. If the infecting organism or its products are in sufficient amount the actual symptoms of the disease appear in the form of what may be termed an acute or subacute anaphylaxis. This condition is prevented or lessened in severity if desensitisation is done early in the course of the infection and the gross symptoms are consequently lessened, although in all cases the infection is not eradicated. In putting forward any actual claim for this method of therapy, one must do so with diffidence, as the work is only in its initial stages. It must be remembered also, that a certain amount of benefit will be derived in these cases by reason of the dietetic and hygienic treatment and by local treatment with mild antiseptics.

When these considerations are weighed up and their effect noted in control cases, one can, I think, conclude—

(1) That by this method a much more potent dose of a specific vaccine may be given in acute, subacute, and chronic infections, without producing hypersusceptibility.

(2) That the gradual processes of immunity are not hindered by desensitising the patient.

(3) That in early acute urethral infections this method will often abort the infection.

(4) That it will rapidly ameliorate acute complications occurring in a subacute or chronic process.

(5) That it will lessen in a considerable percentage of cases the gross clinical signs and symptoms.

(6) That cases in which the signs of disease are alleviated may possibly become carriers of infection.

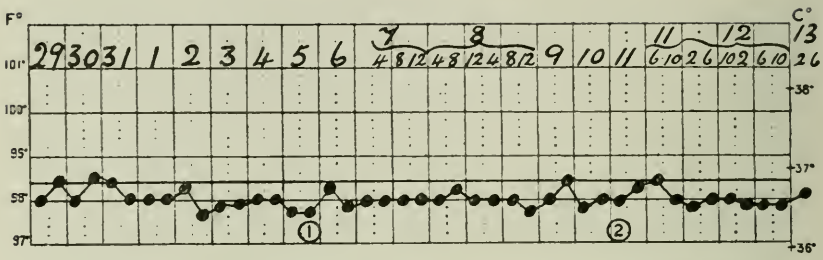


CHART I.—Showing slight reactions subsequent to desensitisation with Autogenous Vaccine.

(1) Intravenous injection of 5000 organisms, Staphylococci, Diphtheroids and Coliform Bacilli. Intramuscular injection twenty minutes later of 250 million of the same vaccine.

(2) Intramuscular injection of 500 million of the same vaccine.

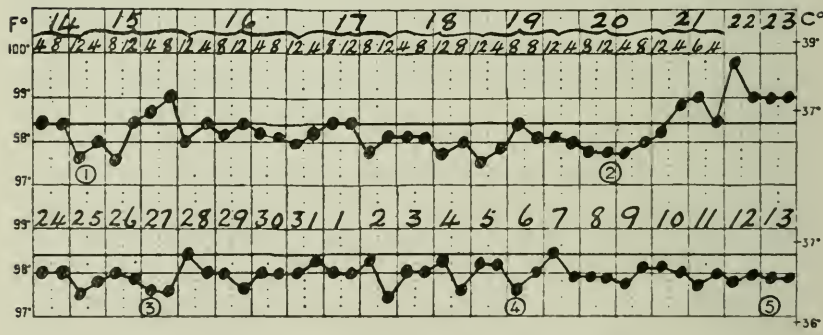


CHART II.—Showing slight reactions after desensitising with Polyvalent Detoxicated Gonococcal Vaccine.

(1) Desensitised intravenously with 5000 organisms. Intramuscular injection of 20,000 million given fifteen minutes subsequently.

(2) Second massive dose of 20,000 million.

(3) (4) and (5) Repeated massive doses of 20,000 million at intervals.

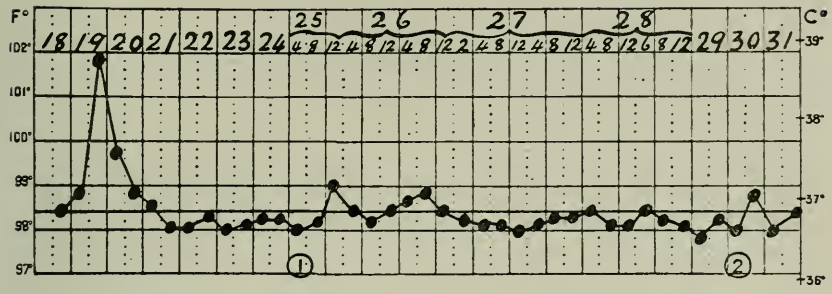


CHART III.—Showing slight reactions in Epididymitis case with Gonococcal and Diphtheroid infection.

(1) Desensitising dose of Polyvalent Detoxicated Gonococcal Vaccine, 5000 organisms, and Autogenous Gonococcal and Diphtheroid Vaccine, 500 organisms.

Curative dose of 20,000 million Detoxicated Gonococcal Vaccine and 500 million Autogenous, given twenty minutes subsequently.

(2) Curative dose repeated.

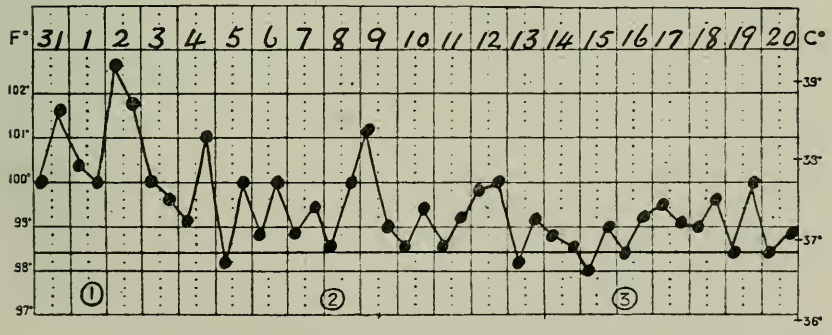


CHART IV.—Showing reactions in case of Acute Multiple Arthritis with Keratodermia. Figs. I. and II.

(1) Desensitised subcutaneously with Detoxicated Gonococcal Vaccine, 5000 organisms.

Curative dose of 20,000 million organisms given two hours subsequently.

(2) and (3) Curative doses of 20,000 million repeated at intervals.

Discussion.

The President, *Sir Robert Philip*, congratulated Mr Lees and the Society on the communication which seemed to him of far-reaching interest and significance. Mr Lees had stated his claim with moderation, in connection chiefly with his own department. It was none the less clear that, if the claim were justified, the principles and methods were capable of wide application. Little had been said as to control observations, but he supposed that Mr Lees had, in contrast with the cases quoted, very many cases which had been subjected to other forms of treatment. Assuming the scientific basis of the method to be assured, its possible extension of application was obviously very wide.

Mr D. M. Greig said that it was now some years since Mr Lees' and Thomson's papers on the use of detoxicated vaccines in gonorrhœa had been before the profession, and he had watched very carefully for corroborative evidence from other workers. Such evidence had not been forthcoming. The text-books mentioned the method, but to a great extent Thomson and Lees stood alone, or comparatively so, in their advocacy. Mr Lees had not, he thought, clearly stated whether other medicinal or local treatment had been used along with the vaccines. He thought it common experience that in the early stages of an acute gonorrhœa, the efficient washing out of the anterior urethra cleared off discharge and removed all pain in one to three days. The effect was most striking, but he could not claim that all fear of a relapse could be removed within three weeks. A weak solution of protargol he had found specially useful, but permanganate of potash was probably equally efficacious. The question was, does Mr Lees continue to use the wash-out of the urethra during his treatment, and if so, for how long? Another question he would like to ask Mr Lees, was as to what guides him in the dose he is to employ in any case. Is it the body-weight of the patient, the virulence of the gonorrhœa, extraneous circumstances, or what?

Professor Ritchie said that Mr Lees' paper had interested him greatly. Its outstanding feature was that, from beginning to end, it had been conceived in a scientific spirit and had been carried out with due regard to all the recognised principles of scientific evidence. The central question in the paper was whether the curious and inexplicable possibility of desensitising patients or animals against a toxic protein could be applied to vaccine therapy, and whether sensitisation was a factor in bacterial infections. The paper fell in line with the work which had been done in the past years, not only on infection, but on sensitisation to proteins. The conception of an animal becoming sensitive to a substance to which, under ordinary circumstances, it was

not sensitive, was one of the great principles which had been emerging in medicine during the last few years, and it might be expected that sensitisation by an infecting organism probably played a far greater part than had been supposed in the processes of disease. The fundamental experiment on which the conception rested was, that if one injected into a guinea-pig a horse serum it had no effect upon the animal, but if after an interval of ten days the same quantity of horse serum was injected the animal might die in the course of a few minutes. The idea was, that the first dose had had effect upon a harmless substance changing it into a poisonous one. He said that he could never understand the effect of vaccines upon acute infections, *e.g.*, acute puerperal infections, and acute scarlatinal infections on the supposition that the vaccines were stimulating some immunising capacity in the body. It was more likely that the effect of the dose of the vaccine was to desensitise. If Mr Lees could establish that by the injection of these small doses, he could obtain a good effect by subsequent large doses, this must be accepted as a clinical fact. More and more, as work on infection went on, it was becoming clearer that the escape of organisms from a local infection into the body was much more common and occurred to a far greater extent than hitherto supposed, and it would be interesting to know whether there was any relationship between the efficiency of Mr Lees' method of treatment and the escape of organisms from the local infection into the general circulation. A study of the degree of this escape and of the course of its occurrence might throw light on the relative parts played by immunisation and by desensitisation in explaining the clinical data. This was not a question which arose only in gonorrhœal cases—it affected vaccine therapy generally, and had a profound bearing on the whole pathology of infection.

Mr Caird was impressed by the large field which Mr Lees' communication had covered. Limiting attention to the treatment where Neisser's organism was active, it would be of practical importance to know what was the average duration of the suggested treatment, and what was the direct evidence of cure and its certainty.

Dr Cranston Low asked Dr Lees if he had ever considered the question of the specificity of his vaccines, because it was possible that any kind of bacterial protein would give the same results. It is a question whether the symptoms of disease are due to the process of immunity-production or whether they are due to the sensitisation of the tissues to the bacterial proteins and not directly connected with the process of immunity. He suggested that Mr Lees should try staphylococcal vaccines in gonococcal cases and see if he got the same result as with gonococcal vaccines. He added a note of warning

against expectations of too great results from vaccines in all diseases. He believed that in some chronic diseases, such as tuberculosis and syphilis, an absolute immunity was never gained. In the former disease the organisms always remained in the body and were never completely removed from the tissues, and therefore in his opinion no form of tuberculin would ever be able to cure tuberculosis.

Mr Lees, in reply, agreed with the President that its application to other domains of medicine and surgery was of importance. He was ready to admit that every case is not successful, and that there are at times disappointing results.

With regard to the question of controls, simultaneously with the cases which have been reported, there were under observation many cases treated by various other routine methods which did not show the same remarkable results. He could not say in connection with any of these cases which had shown those rapid results subsequent to desensitising, that the same cases would not have recovered as quickly under different treatment. It was perfectly true that certain cases of gonococcal infection was automatically cured, but they are few in number, and it is very rarely in the average case that the gross symptoms of the disease disappear so rapidly as they did in the majority of this series.

Mr Greig had raised the whole question of vaccine therapy and corroborative evidence by other workers. At the discussion on the treatment of gonococcal infection at the British Medical Association Meeting in July last, there was a general consensus of those present that better results were obtained by detoxicated vaccines, when used in conjunction with local mild antiseptics, than by any other single method. Harrison, Buckley, Ffrench, M'Donagh, and others have all spoken of their value in infections of the lower urinary tract, and when used scientifically they are distinctly beneficial.

With regard to the question of the other treatment adopted, in the cases which were aborted, only mild antiseptics were used, chiefly a solution of 1/8000 to 1/10,000 potassium permanganate and usually only once daily, and Mr Lees did not think it was the experience of most workers that this alone would abort even an early urethritis.

Professor Ritchie had raised a very difficult and thorny question—"Can this desensitising dose against a toxic protein, in patients or animals, be applied to therapy to induce tolerance to a later massive dose?" From observation of cases Mr Lees thought so. He had on one occasion applied the same principle in administering novarsenobillon in a case of angio-neurotic œdema. The phenomenon is difficult to explain unless one is prepared to accept the suggestion of Danysz, that the patient is passing through a period of sensitisation during the incubation period of his disease.

In reply to Professor Caird's question, "Does it end in cure and how long does the cure take?" Mr Lees mentioned the possibility of some of these patients becoming carriers, the cure being apparent and not a real one. Certainly a considerable number of them are cured, and cured rapidly, but in all it is essential to observe for a long period to make certain of cure, and the cases which are an apparent and not an absolute cure do not seem to take any longer to clear up than they would by other methods, and the acute period of their disease is much shorter.

Referring to Dr Cranston Low's scepticism as to the specificity of the process and his suggestion that any protein might act similarly, Mr Lees said he had seen results in isolated cases from protein therapy in gonococcal infections but rarely without acute reactions being set up by the protein. This is seen, for example, in the use of typhoid vaccine and antidiphtheritic serum in gonococcal arthritis, and there is now a consensus of opinion that better results are obtained with less danger to the patient by using a specific serum or vaccine to treat the joint complications of gonorrhœa. The others are erratic in their action and quite empirical as, for example, the use of manganese and pallamine. He was surprised to hear the statement made that chronic diseases never cure, and he thought that in most domains of medicine and surgery curative results have been obtained in some very chronic diseases by vaccine therapy, when properly applied. Administration of a vaccine is not however the one and only method of aiding in the elimination of disease. It is a useful adjunct to other methods and if carefully and scientifically administered is often helpful in clearing up resistant infections.

Mr Lees was only too ready to admit the disappointments which one meets with in its use, but we have in it a potent weapon which, if properly applied, and with increasing knowledge of the processes of immunity, may be more taken advantage of. It was with this aim in view that he began this, as yet, experimental work.

SPECIAL CLINICAL MEETING.*

Sir ROBERT PHILIP, *President, in the Chair.*

DEMONSTRATIONS.

Dr Chalmers Watson gave a **histological demonstration of the blood** in primary anæmia from the patient exhibited by him at the Clinical Meeting, and of other blood conditions from patients in the wards.

Professor J. Meakins gave a demonstration, in the Biochemical Laboratory, of **disturbances of respiration,** with reference to (*a*) Cyanosis and its relief; (*b*) Consequences of respiratory resistance; (*c*) Cheyne-Stokes breathing and its relief; and (*d*) Basal metabolism.

Mr Charles W. Cathcart gave a demonstration of **Thomson's Apparatus**, worked by the feet, for the use of armless men.

The use of this apparatus was demonstrated by Mr Alex. Waugh, a former patient of the Infirmary, who lost both arms by a live electric-wire accident some years before the war.

By the aid of this unique apparatus, invented and made by Mr George Thomson, Edinburgh, Mr Waugh can now feed himself, using knife, fork, and spoon; drink from a cup; pick up a cigarette and light it; write an excellent "hand"; and help himself in many other ways which without it would be impossible.

EXHIBITION OF PATIENTS.

Medical Patients.

Dr Rainy showed a case of **Enlargement of the Spleen.** H. S., a schoolboy, æt 14. After an accident he developed dysarthria early in 1921. This gradually got worse and was found to be associated with paresis of the soft palate and some weakness in the lingual and labial musculature. This led to his admission to the Royal Infirmary, where it was found that there were signs of early pulmonary tuberculosis in a quiescent state. The diagnosis was therefore suggested that the dysarthria was probably due to some tuberculous focus in the neighbourhood of the involved cranial nerves or their nuclei. In March 1922, he was brought back to the Infirmary because of a severe hæmatemesis, and it was then discovered that the spleen had become much enlarged and extended for a considerable distance beyond the costal margin. The enlargement was uniform, the surface smooth, and no nodules or irregularity could be

* Held in the Royal Infirmary, 17th May 1922.

detected. There were no indications of any abdominal tuberculosis and the spleen was much larger than one would expect were it due to tubercle. The diagnosis that seemed most in keeping with all the facts was one of Banti's disease occurring in an individual who was already the victim of organic nervous disease which was showing a tendency to spread, and which was probably of a tuberculous nature. In these circumstances, splenectomy was contra-indicated unless grave symptoms should supervene.

Dr Chalmers Watson showed a case of pronounced **Primary Anæmia,** developed in the course of treatment for syphilis, raising the interesting question as to the relationship of the anæmia to (*a*) the specific infection; (*b*) the influence of arsenic administration (N.A.B.).

Examination of the fæces and the urine (Mr Kermack) showed the presence of arsenic in both excretions fifteen months after cessation of arsenic administration.

The President showed—(1) a case of **Endemic Hæmaturia (Bilharziasis).** The patient, a student at Edinburgh University, suffered from loss of flesh and working capacity. Examination revealed the presence of hæmaturia and pyuria. The urine contained no tubercle bacillus or other organisms of importance. Following simple treatment and a holiday the patient gained some 14 lbs. in weight. On subsequent examination, hæmaturia and pyuria were found to continue. Tubercle bacilli were not present, but ova of Schistosoma Hæmatobium were discovered in considerable numbers. Before coming to Edinburgh the patient had lived in Egypt.

(2) Two cases of pronounced **Tuberculosis, illustrating the value of Tuberculin exhibited externally by inunction.**

(*a*) A lad of 18½, postman, under treatment at Southfield Sanatorium Colony. Patient has had genito-urinary symptoms for four and a half years. On detailed examination in February 1918 he was pale, thin, and markedly toxæmic. He looked very ill. There was great frequency of micturition—forty-eight times in the twenty-four hours—with considerable pain on each occasion. The urine contained blood, pus, and tubercle bacilli. Later, the right epididymis was found involved and the right cord thickened, with a discharging scrotal sinus. There were other minor evidences of tuberculosis.

Following treatment by tuberculin (inunction 50 per cent. at varying intervals and for prolonged periods in the manner Sir Robert had suggested a good many years ago), a satisfactory result was gradually obtained. To summarise: the genito-urinary symptoms had

quite disappeared; micturition now five times in the twenty-four hours; quantity natural, and no abnormal content. The affection of epididymis was hardly determinable, and there was a gain in weight of 28 lbs.

(*b*) A young man of 23, labourer, referred to Tuberculosis Clinique in May 1921 by Mr D. P. D. Wilkie, and admitted to Southfield Sanatorium Colony in July 1921 on account of extensive abdominal tuberculosis. Mr Wilkie had opened the abdomen and discovered the presence of a large mass of great density, occupying the pelvis and lower part of abdomen, almost completely immobile, and apparently attached to the anterior surface of the sacrum. Nothing could be attempted in the way of removal. Histological examination showed the tumour to be of tuberculous nature.

He was treated for a couple of months in the Medical House and then transferred to Southfield Sanatorium Colony. In addition to more general measures the patient was treated by tuberculin (*inunction method*).

The huge mass, which extended an inch and a half above the umbilicus, with much tenderness at the higher level and vesical symptoms, was gradually reduced in size. After ten months, the abdomen is practically natural in appearance and consistence, and all symptoms have disappeared. There is at present only a trace of resistance passing in band-like fashion from the right iliac fossa. The patient, who on admission was pale and thin and unable to stand upright, now presents a robust aspect, does a full day's work, and has gained 3 stone in weight.

Dr N. S. Carmichael showed a case of **Bronchiectasis**. Annabella S. aet. 2½ years. Admitted to hospital six times suffering from broncho-pneumonia. After the third attack signs of interstitial pneumonia developed.

Her present condition:—Shrinking of the left side of the chest. The whole of the left lung involved a well-marked cavity in the upper part of the left lower lobe. Right lung affected in a much lesser degree. Heart drawn over to the left side. Marked "clubbing" of the fingers and toes. Slight cyanosis. Paroxysmal cough. Sputum mucopurulent, foul odour. Tubercle bacilli never found. Organisms present—M. catarrhalis, pneumococci, pneumo-bacilli, streptococci, and staphylococci. Von Pirquet and Wassermann reactions negative. X-ray photographs show no sign of foreign body.

Dr Eason showed a case of **Oxycephaly** in a boy aet. 9 years. The boy is a twin and was shown with the normal brother. The comparison was very interesting as demonstrating that the oxycephalic boy was, generally speaking, equal to his brother in growth and development. The oxycephalic boy suffered from frontal headaches after physical or mental exertion and had consequently been unable

to attend school, or to engage in out-door games; he had, in all, spent three months at school. If he moved about quietly and had no form of emotional excitement he had no headache, but the face easily flushed and he suffered from headache if for any reason he became angry. The oxycephalic features that were well marked in the case were the very high pointed vertex, the prominent eyes, the poorly-developed supraciliary ridges and frontal eminences. The X-ray photograph showed well the abnormal form of the skull and also demonstrated the extreme thinness of the cranium, so that the moulding on the internal surface caused by the cerebrum—the so-called "digital" markings were seen. The attention of the Society had recently been drawn by Mr Greig to the effect of the cranial deformity on the jugular foramina. These were so small that other and unusual routes had to be provided for the return of blood from the brain. The boy shown had abnormally large veins about the left eyelids passing towards the left ear. There was also a small communication between the scalp and the anterior part of the saggital suture, as seen by the veins in the middle of the forehead.

There were some negative points of interest. A casual glance did not reveal any striking abnormality of the head and face. One of the most striking features in oxycephaly was entirely absent, viz., the tilting of the orbital cavity, so that from the nasal side it dropped to the temporal. The absence of this feature and the present long crop of hair on the head which concealed the deformity of the vertex masked the condition of oxycephaly. There was also no deformity of the hands and the boy did not seem mentally inferior to his brother, who was able to take a good place at school.

Mr Greig had kindly given his opinion of the case, and had reported that the boy was one of the slighter cases of true oxycephaly. He was of the opinion that there had been premature fusion of the coronal suture at its lateral extremities and premature fusion of the basilar suture so that the basilar process remained unduly small.

Surgical Patients.

Professor Alexis Thomson showed a case of **Ruptured Axillary Artery and Gangrene of Forearm.** The patient, a slater, æt. 54, was admitted on 6th January 1922 to Ward 13, R.I.E., from Dr Beveridge, Kirkcaldy. He was skylarking with other men after some drinks in a public-house, when he is supposed to have fallen on the pavement with the hand under him. This was between 3 and 4 P.M. on the 5th January.

When the doctor saw him an hour or two later he recognised a dislocation of the humerus, an enormous swelling in the axilla, and that the limb was cold and pulseless, evidently the axillary artery had

been ruptured at the same time as the bone was dislocated. The doctor failed to reduce it without chloroform, but succeeded after this was given. He suffered great pain through the night. Next morning the shoulder and side of the chest were enormously swollen and bluish-black in colour. There was some drop wrist and loss of sensation in the fingers. There was no pulsation in the radial or brachial arteries.

The X-ray showed that the dislocation had been reduced. His further progress was attended with increase in the swelling from extravasated blood and gradual gangrene of the hand, extending to the junction of the upper and middle thirds of the forearm. He still suffered an enormous amount of pain, did not sleep without morphine, and threatened suicide unless we could relieve him.

On the 8th March at the urgent request of the patient the limb was disarticulated at the elbow. He improved after this but the stump healed badly, as if there was no proper innervation of the tissues, and massage had little effect in dispersing the extravasated blood. As, further, the temperature had begun to go up again, and the skin showed signs of giving way, on the 8th March Professor Alexis Thomson opened up the axilla, turned out the clots, and, finding the artery actually bleeding at the time, it had to be tied above and below the seat of rupture. The wound was packed and firm pressure applied in the abducted position.

There is still a discharging sinus in the axilla, and the movements of the upper arm and stump are extremely limited.

Mr Thomson regretted that he had not cut down on the artery when the man was admitted to hospital.

Mr Scot Skirving showed (1) a patient, male, æt. 34, after drainage of huge **Mesenteric Cyst.** Case shown a year ago before operation (as a case for diagnosis) to Medico-Chirurgical Society and also to Association of Surgeons of Great Britain. Swelling first noticed six years ago. Grew steadily. No symptoms: carried on his work as labourer until three weeks before operation (May 1921), and only ceased work then because of the inconvenience of the swelling. No special hydatid antecedents. Wassermann negative. No thrill: swelling continuous with liver and extended to within two inches of Poupart's ligament and across middle line two and a half inches to left. Diagnosis lay between hydatid and mesenteric cyst. At operation twelve pints of turbid, brownish, highly albuminous fluid evacuated, containing much cholesterin, many polymorphs, red-blood corpuscles, and endothelial cells. No hydatid contents: no organisms on staining or culture. The cyst wall was intimately attached to the cæcum, ascending and transverse colon, and for this reason it was found impossible to excise the cyst without also resecting these parts. It

was also adherent to the lower surface of the right lobe of the liver. It was, therefore, simply treated by drainage. A small sinus still exists after a whole year's drainage. The discharge (chiefly purulent) from this amounts to about a teaspoonful in the twenty-four hours. Otherwise the patient, who has been back at work for some months, is in good health. A portion of the cyst wall removed for microscopic examination showed dense fibrous tissue with hæmorrhages in places, and much small round cells and fat cells round the vessels.

(2) A boy, æt. 13, after **Ligature of Popliteal Artery for Repeated Secondary Hæmorrhages** following acute osteomyelitis of tibia in which other means of arresting the bleeding had failed.

Admitted with condition of tibia so bad that almost whole shaft had to be excised. Some days later hæmorrhages began. Exact site of bleeding difficult to localise—a general ooze from neighbourhood of upper extremity of wound, mostly from upper end of the divided tibia. Packing, elevation of limb, injection of horse serum (intramuscular), intravenous transfusion of blood from a brother, all failed. Eight hæmorrhages in all over a period of some weeks. Profound secondary anæmia present. Question of amputation or ligature of popliteal artery? Circulation of foot very feeble, but thought best to try ligature first. This proved completely successful. No history of hæmophilia.

Case shown as an example of one of the possible sequelæ of excision of a long bone for acute osteomyelitis, and of the difficulty sometimes of treating such hæmorrhages.

Mr J. W. Struthers showed—(1) Male, æt. 54, after recovery from an illness due to the formation of a false or **Traumatic Pancreatic Cyst** following a severe blow on the upper abdomen from the buffer of a railway wagon on 28th November 1921. A moderate degree of shock with diffuse pain and tenderness in the abdomen followed the injury but passed off in a few days and the patient was discharged from hospital, apparently well, on 7th December. On 12th January 1922, forty-five days after being injured, he was re-admitted with a large fluctuating swelling in the right upper quadrant of the abdomen. This was opened and found to contain a colourless limpid fluid encysted in the general peritoneal cavity. The cavity was drained. Fluid escaped at the rate of about 550 c.c. in twenty-four hours, for several weeks. It then lessened in amount gradually, and finally ceased to flow on 6th March, thirty-nine days after the cyst was opened. The fluid was found to contain all the pancreatic ferments and caused a great deal of irritation of the skin. In spite of the escape of so much pancreatic fluid the patient's capacity to digest fat, as tested by analysis of the stools after ingestion

of a known quantity of milk, was not affected. After the drainage opening closed the patient remained well.

(2) Male, æt. 42, who had had recurrent attacks of painful dyspepsia for years culminating in a severe hæmatemesis and melæna, pointing to the existence of a **Duodenal Ulcer.** On opening the abdomen no sign of ulcer could be seen or felt on examining the outer aspects of the duodenum and stomach, and the viscera appeared perfectly healthy. On opening the stomach, however, and examining the duodenum with the index finger passed through the pylorus, a shallow ulcer was found on the upper aspect of the duodenum. The case illustrated the liability to error if conclusions are drawn from examination of the outer aspect of the viscera alone.

Mr D. P. D. Wilkie showed two cases of **Duodenal Ulcer complicating Chronic Duodenal Ileus** treated by gastro-jejunostomy and duodeno-jejunostomy. (1) Male, æt. 29. Complaint: recurring attacks of vomiting and epigastric pain of three years' duration. The attacks came on suddenly at intervals of two to three months, and lasted for from two to five days. Vomiting was the initial symptom in each attack accompanied by pain, which was maximal about two hours after eating. The attacks were usually promptly relieved by rest in bed, but without rest in the recumbent position medical treatment gave no relief. A feature of each attack was the prostration and loss of weight which it produced. The last attack was the most severe one; bilious vomiting continuing for five days. A diagnosis of chronic duodenal ileus was made and operation recommended.

On opening the abdomen a greatly dilated first portion of duodenum presented and when the transverse colon was lifted up the third part of the duodenum was also found to be dilated and bulging. A stomach tube was passed and the stomach inflated. The gas passed freely through the pylorus and filled the dilated duodenum but did not pass beyond the root of the mesentery, and the jejunum remained collapsed. When, however, the mesenteric vessels were raised on the finger the gas readily passed on. A small "shirt-button" ulcer was seen on the anterior wall of the first part of the duodenum and another on the posterior wall, just beyond the pylorus. A posterior vertical gastro-jejunostomy was performed and in order to drain the dilated duodenum an anastomosis was made between its third part and the jejunum, seven inches beyond the gastro-jejunostomy. There was no vomiting following the operation, and now, five weeks later, the patient has gained one stone in weight.

(2) Male, æt. 42. Complaint: Flatulent dyspepsia for about twenty years. After a meal he suffered from a feeling of great distension in the epigastric region, which was relieved by belching

up wind and making himself vomit. Five years ago he began to have attacks of pain of the duodenal ulcer type. For the past year pain and flatulent distension have never been absent and have been relieved hardly at all by rest in bed and milk diet. X-ray examination showed a dilated stomach and eight-hour gastric retention. The cachectic appearance of the patient led to a provisional diagnosis of gastric carcinoma.

On opening the abdomen the first part of the duodenum protruded, showing a remarkable dilatation. The pylorus was patulous, admitting three fingers; the second and third parts of the duodenum were equally dilated, the first coil of jejunum was collapsed. On the posterior wall of the first portion of the duodenum was a large indurated ulcer with evidence of subacute perforation. A posterior vertical gastro-enterostomy was performed and an anastomosis made between the retro-peritoneal third portion of the duodenum and the jejunum, seven inches beyond the gastro-enterostomy.

A rapid and uneventful convalescence was made, and now, seven weeks after operation, the patient has gained more than one stone in weight and has a normal and healthy complexion.

Dr Traquair showed a case of **Repair of the Upper Eyelid** after a severe burn of the right side of the face four months previously. Practically the whole of the skin of the upper lid was absent, the eyelashes being intermingled with the hairs of the eyebrow. The conjunctiva was everted and swollen, forming a large red projecting mass. The lower lid was similarly drawn down by contracted scar tissue, exposing nearly the whole of the lower conjunctiva. The lids could not be closed. No healthy skin being available in the neighbourhood, a large flap, involving the whole thickness of the skin, was taken from the left arm and applied to the raw surface left after free dissection of the upper lid. The graft took completely and a well-formed upper lid is now present, permitting of complete covering of the eye. The lower lid remains to be dealt with similarly.

OXYGEN-WANT: ITS CAUSES, SIGNS, AND TREATMENT.*

By JONATHAN MEAKINS.

It is not my intention in my communication this evening to discuss in detail the various pathological or structural changes of the lungs of which we are all familiar, but to devote my time to discussing how these various structural changes influence the respiratory function. By the function of respiration I mean respiration in general, not only the respiration as interpreted through the lungs themselves but also respiration as it finally bears upon the tissues of the body. Now a structural change of the lungs may or may not lead to a very gross interference with their function, and as far as the respiratory function is concerned an anatomical change is only of importance when it interferes with this function. In order to draw an analogy I might point out a close resemblance between the functional efficiency of the circulation and the efficient function of the respiratory system as a whole. It is well known to all of you that there may be a more or less pronounced lesion of the endocardium or of the valves of the heart and still the circulation may be carried on in an efficient manner. In the same way you may have a gross lesion of the respiratory system, as for instance a complete one-sided pneumo-thorax from which to all intents and purposes the individual experiences no distress or symptoms. On the other hand, if the change of structure interferes with function the evidence of such may be felt at rest or may be appreciated on trying to undertake certain work.

The first point to be considered is how the blood normally acquires oxygen and gets rid of carbon dioxide. The main function if not the only function of the blood in regard to respiration is that it shall acquire oxygen and give up carbon dioxide, in other words it shall change from venous blood into arterial blood. If normal blood is exposed to oxygen at body temperature it will acquire oxygen after a peculiar manner (Fig. 1). The abscissa represents partial pressure of oxygen in the air to which the blood is exposed and ordinates represent the percentage saturation of the oxyhæmoglobin. You see that the curve is one of a peculiar shape which is of very great

* Read 5th July 1922.

importance. The normal alveolar air to which the blood in the alveoli is exposed represents about 100 mm. of oxygen which saturates arterial blood to about 95 per cent., and from then on it is practically a straight line, with very little increase in the saturation. Even if it be exposed to 150 mm. partial pressure of oxygen it will only be about 99 per cent. saturated.

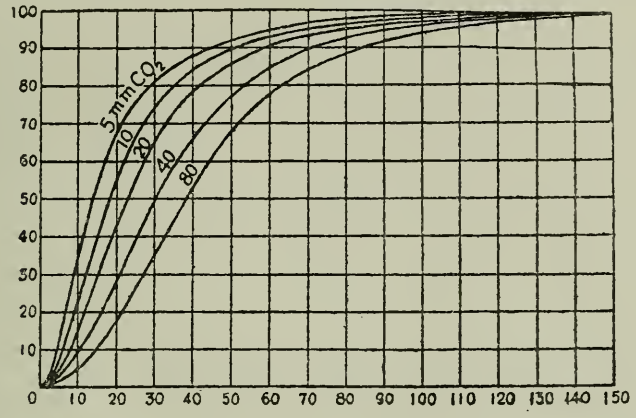


FIG. 1.—Curves representing the percentage saturation of hæmoglobin with oxygen at different partial pressures of oxygen and CO_2. Dog's blood at 38°C. Ordinates = percentage saturation with oxygen; abscissæ = partial pressures of oxygen in millimetres of mercury. (Bohr, Hasselbalch, and Krogh.)

On following these curves to the left you find that soon there is a sharp decline which is of extreme importance, in that for a very small fall of oxygen pressure a relatively large amount of oxygen is given up. Not only does the circulating blood contain oxygen but it also contains carbon dioxide, variation of which operates in a very efficient manner in helping the blood to obtain or give up oxygen. The curve marked 40 mm. pressure of carbon dioxide represents that of arterial blood as subjected to the alveolar air. Now as the carbon dioxide diminishes in concentration so the blood takes up more oxygen, and as the carbon dioxide increases in percentage or concentration so the blood takes up less oxygen, or conversely, gives up more oxygen for a given change in oxygen pressure. This is of extreme importance in the tissues. The arterial blood as it leaves the alveoli has been exposed to 100 mm. pressure of oxygen and 40 mm. pressure of carbon dioxide, and as a consequence is saturated to 95 per cent. of its capacity. On the other hand, when it goes to the tissues it meets

naturally a demand for oxygen and an increased concentration of carbon dioxide, which results from the production of energy and consequent increased consumption of oxygen. Oxygen is consumed and carbon dioxide is given up, therefore on account of the latter fact the blood gives up what oxygen it has more readily. When it returns to the lungs it gives up carbon dioxide to the inspired air where there is only 0·03 per cent., and thus acquires its oxygen more easily. So there is a perfect balance between the acquisition of oxygen on the one hand and the giving up of carbon dioxide on the other, and then when blood reaches the tissues it gives up its oxygen more readily. This follows from the fact that the oxyhæmoglobin curve varies according to different pressures of carbon dioxide and the carbon dioxide dissociation curve varies with different pressures of oxygen. Thus it is so arranged that the interchange of gases between the blood and the alveolar air and the blood and tissues takes place with the greatest ease and minimum variations of gaseous pressures. The difference of gases between arterial and venous blood is merely the difference in the concentration of oxygen and carbon dioxide, arterial blood having a higher oxygen content and lower carbon dioxide content, while the venous blood is vice versâ.

In Fig. 2 are shown curves of a normal person (upper) and a patient (lower) showing a very pronounced degree of cyanosis, and no other symptoms. She was referred to me by Professor Gulland and led to a great deal of mystery and cogitation, until these observations were made. I am indebted for the complete curve to Mr Barcroft, F.R.S., of Cambridge. It is really a most exceptional case, yet I hope it will explain why the patient had cyanosis without other symptoms. You will readily note the difference in the two dissociation curves. The lower one is that of the patient. The arterial blood going to the tissues was deficient in oxygen, therefore there was pronounced cyanosis. On the other hand this type of curve makes it quite clear that although the blood was deficient in oxygen it would give up what it had with much less difficulty. She was supplying her tissues with plenty of oxygen, although as the arterial blood left the lungs it was deficient in oxygen. It is not the oxygen of the oxyhæmogoblin which matters but it is the amount of oxygen which the plasma has in solution that matters. As the plasma comes into contact with the tissues through the capillaries it gives up its oxygen to the cells which

is constantly using oxygen to do their work, therefore there is continuous cry for more. As the plasma passes about the cells, the cells take from the plasma what oxygen it has in solution. As a consequence the partial pressure of oxygen in the plasma falls and the oxyhæmoglobin immediately sheds its oxygen into the plasma so that there is a constant supply of oxygen from the hæmoglobin into the plasma and from the plasma to the

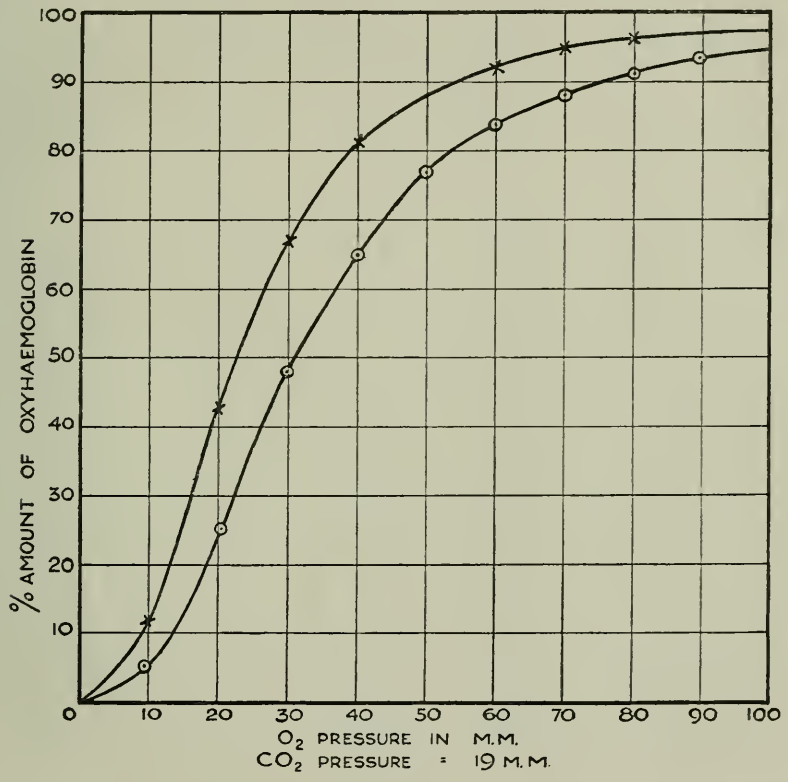


Fig. 2.

cell, and it is the concentration of oxygen in the plasma that counts as far as the tissues are concerned.

The venous blood as it returns to the heart is about 75 to 80 per cent. saturated with oxygen, while the arterial blood as it leaves the lungs is nearly 95 per cent. saturated, so that on the average during the circuit of the blood over 15 per cent. of its oxygen has been consumed. If the tissues for any reason are deprived of this supply of oxygen, we term it "oxygen-want." It is to this condition and its results that I want to

draw your attention. In the first place, I would like to point out in brief the causes of oxygen-want (Table I.), which really means the lack of oxygen for the proper nutrition and the proper work which the tissues must carry out.

TABLE I.—*Causes of Oxygen-Want.*

A

Atmospheric air . .	Low O_2 per cent.—Low barometric pressure.
Trachea and Bronchi .	Obstruction—internal and external—tumour—spasm, etc.
Alveolar epithelium .	Œdema, thickening, inflammation.
Blood	Anæmia, CO poisoning. Failure of blood to give up oxygen.
Admixture of arterial and venous blood . .	Unequal pulmonary ventilation. Congenital heart disease.

B

Circulation . . .	Slowing.
Tissues	Cyanide and sulphuretted hydrogen poisoning.

In the first place, if the barometric pressure be reduced the available oxygen is proportionately reduced even though the percentage remain the same, as it is the pressure of oxygen which counts. (20·9 per cent. oxygen at one half an atmosphere barometric pressure equals practically the same as 10 per cent. oxygen at one atmosphere barometric pressure.) So if the amount of oxygen in the inspired air, as in blackdamp in mines, is greatly diminished, the organism will suffer acutely. On the other hand, at a very high altitude, as Paul Bert pointed out, it is not the percentage of oxygen but the partial pressure which is important. If there is half the oxygen at sea-level, it gives the same result as if there was normal air but half the barometric pressure. If it be quarter—it is the same as if you were at an altitude of quarter the barometric pressure of sea-level. So with changes of atmospheric air, whether the oxygen is diluted, or the barometric pressure is diminished proportionately, the end result is the same.

Another cause is found in any obstruction either internal or external of the trachea or main bronchi which act but as a conducting system for the lungs. A tumour pressing on the trachea, the membrane in laryngeal diphtheria, a spasm of the bronchioles as in asthma, or the intense swelling of the mucous membrane in certain types of suffocative bronchitis, or croupous-pneumonia, all produce the same results. The alveolar epithelium is placed in such a position that it cannot acquire oxygen at the normal partial pressure. Likewise in œdema of the lungs, the

swelling of the cells and the presence of exudate prevents the oxygen getting through to the blood as readily as normally. Likewise in chronic emphysema where there is extensive thickening of the alveolar and capillary wall and epithelium ; in the inflammatory condition present in the early stages of lobar pneumonia and probably throughout the course of broncho-pneumonia there is a direct mechanical interference with the transfer of gases between the alveolar air and the blood. In the next place there may be an actual deficiency of hæmoglobin carrying-power of the blood through a direct lack of hæmoglobin. It can be quite readily understood that the less hæmoglobin there be, the smaller amount of oxyhæmoglobin there will be and therefore the less oxygen will be available for the tissues. In CO poisoning this gas has a greater affinity for hæmoglobin than has oxygen, therefore the amount of oxyhæmoglobin is more or less diminished and in consequence the tissues obtain an insufficient supply of it. In congenital heart disease where there is an incomplete septum or patent ductus arteriosus the arterial blood is diluted with venous blood in a more or less pronounced degree, and in consequence the blood in the arteries approximates to normal venous blood with resulting oxygen-want in the tissues. In congenital heart disease with pulmonary stenosis the oxygen saturation of the arterial blood is normal, but the circulation rate is so diminished that the supply to the tissues is deficient. In addition to such cardiac lesions there is a very important clinical condition resulting from unequal pulmonary ventilation. The lungs are an enormous collection of alveoli, some of which are ventilated more efficiently than others—those of the sub-pleural zone better than the alveoli of the central zone, and the diaphragmatic better than the apical zones. The blood returning from the poorly ventilated alveoli will contain less oxygen than the blood returning from the well-ventilated alveoli. On reference to Fig. 1 it will be seen that in the well-ventilated alveoli the blood cannot take up more than a certain amount of oxygen, while in the poorly ventilated portions it may take up considerably less. In consequence there may be a condition, the end result of which may be similar to congenital heart disease where there is a septal deficiency. The condition is produced in an increasing degree as the respiration becomes more rapid and shallow.

I must now refer to the production of symptoms of oxygen-want in cardio-vascular disturbances. During the last year we

have devoted much time to the investigation of the question of why respiratory symptoms occur in cardiac disease. We have found that shortness of breath occurs although the arterial blood may be normally oxygenated. But we have also found that the quantity of blood supplied to the tissues is much below normal even at rest, and on exertion the amount supplied is proportionately very much less than normal. It is therefore not a question of quality but of insufficient quantity which leads the individual to suffer from oxygen starvation.

Cyanide and Sulphuretted Hydrogen Poisoning.—In these conditions there appears to be a definite change in the tissues so that they are unable to use the oxygen which is supplied. In cyanide poisoning the blood is normally charged with oxygen, but when it reaches the tissues they are unable to use it.

From the preceding examples I hope that I have made it quite clear that oxygen-want must be regarded as an insufficient amount of oxygen in the tissues. It is most important to realise that it is the conditions of the tissues which count, irrespective of the oxygen saturation of the arterial blood. In consequence of the tissues not having sufficient oxygen the signs of want of oxygen appear. The signs of oxygen-want are —*cyanosis*, dyspnœa, orthopnœa, periodic breathing, dulling of special senses, vomiting, diarrhœa, restlessness, delirium, coma, etc.

Table II.

No.	Inspiring Air.	Inspiring Air enriched with Oxygen.	Oxygen per cent. Saturation of 100 c.c. of Arterial Blood.	Cerebral Symptoms.
1	+	–	83	Slight delirium.
	+	-	82	Delirious.
	–	+	91	No delirium.
	–	+	92	" "
	+	–	84	Very restless.
	–	+	97	No delirium.
2	+	-	89	Restless.
	–	+	98	Very comfortable.
3	+	–	80	Semi-comatose.
	–	+	94	Quite rational.
4	+	-	84	Delirious.
	-	+	90	Slightly restless.
5	+	–	81	Semi-delirious.
	–	+	93	No delirium.
6	+	–	79	Delirious.
	–	+	98	No delirium.

In Table II. are shown a number of cases, chiefly of pneumonia, in whom the arterial blood, and as a consequence the tissues, are deficient in oxygen. They all exhibited signs indicating a disturbance of the central nervous system—delirium, restlessness, etc. It was found that as the oxygen content of the arterial blood was raised, by the administration of oxygen, the symptoms referable to the central nervous system disappeared. It will be noted that in all the cases the oxygen saturation of the arterial blood was much below normal, but on adding oxygen to the inspired air the saturation of the arterial blood was brought up to normal.

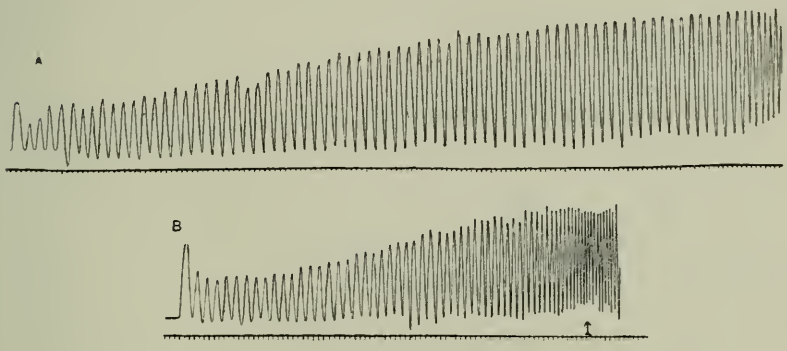


FIG. 3.—Subject Cpl. M.

(*a*) Rebreathing—concertina filled with oxygen—CO_2 accumulating.
(*b*) Rebreathing—concertina filled with air—CO_2 accumulating.
Time marker = 2 seconds. Arrow shows points where lips were distinctly blue.

The next point to be considered is the question of respiratory function under various conditions of oxygen-want.

In the first tracing in Fig. 3 there is shown the effect of breathing a high concentration of oxygen but allowing carbon dioxide to accumulate. The slow and gradual increase of respiration will be noted. In curve B the oxygen diminishes and carbon dioxide is allowed to accumulate simultaneously, and it will be noticed how quickly there is an increase of volume and rate of respiration with cyanosis, which is the usual result produced when low oxygen and high carbon dioxide concentrations occur in the alveolar air.

In Fig. 4 is clearly demonstrated the difference between the type of breathing when one is sitting in a chair and when one is lying perfectly prone. You will notice that when sitting in a chair the breathing is quite regular, but when one lies down

there begins to appear large individual respirations which really are indicative that ventilation of the lungs is not as efficient in the recumbent as in the sitting position. There is also a distinct slowing of the respiration. In sleep the respirations are slow and interrupted at intervals by much deeper

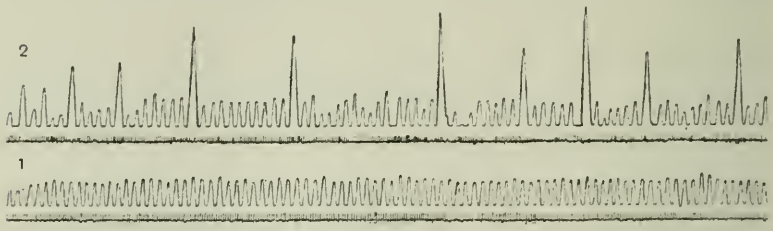


Fig. 4.—Subject J. C. M. Unlimited concertina. Time in seconds.
1. Sitting. 2. Lying.

respiratory movements. Some individuals respond more readily after this manner to this change of position than others do, while it is very interesting to find that normal individuals react at all to this change of position. Children very frequently show a distinct periodicity in their breathing when asleep in the prone position. On continuing this subject many interesting results

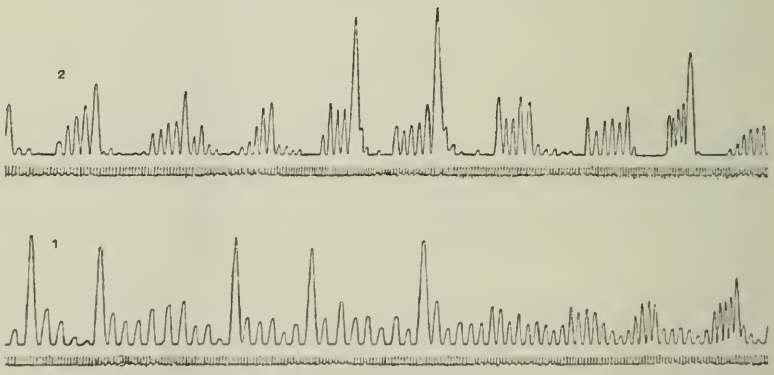


Fig. 5.—Subject J. C. M. Unlimited concertina. Time marker = seconds.
1. Sitting, with corsets. 2. Lying, with corsets.

are obtained. These are shown in Figs. 5 and 6. In the lower curve the subject is sitting in a chair but the breathing is restricted by a very tight corset about the abdomen. You notice the irregular character of this breathing. It is in fact a modified type of Cheyne-Stokes breathing. When the individual assumes the prone position the respiration becomes

much more irregular and the deep respirations are much exaggerated and occasionally the corsets were rent by the violence of these movements. All persons do not respond equally to restriction of the respiratory movements.

In Fig. 6 it will be noted that in the sitting position the respiratory peaks are much more frequent and the breathing is much slower and more irregular, while when in the prone position the irregularity becomes much more pronounced. The direct

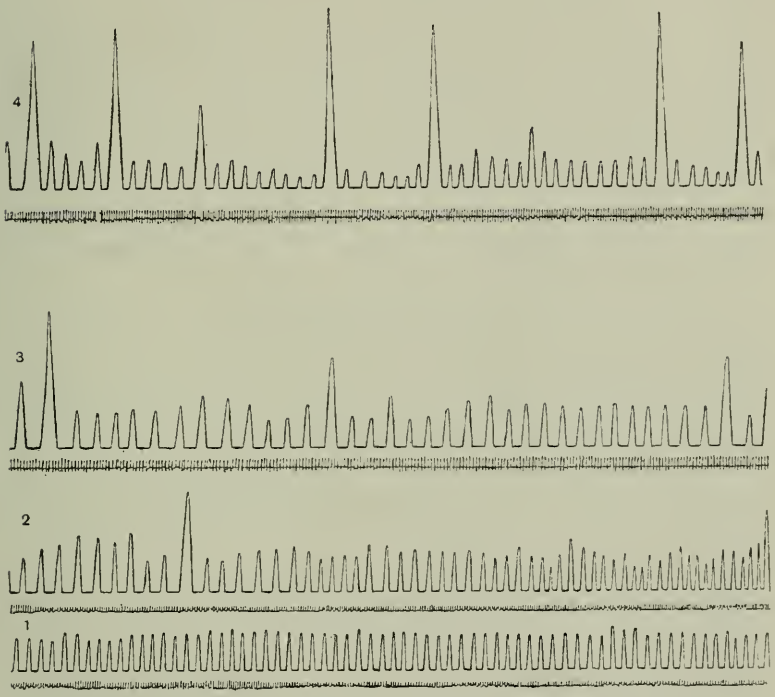


FIG. 6.—Subject J. G. P. Concertina unlimited. Time marker = seconds.
1. Sitting. 2. Lying. 3. Sitting, with corsets. 4. Lying, with corsets.

result of the constriction of the thorax and abdomen is to prevent the diaphragm from exerting its proper movement. The diaphragmatic surfaces of the lung are most efficient from a respiratory point of view, and when its movement is restricted by the pressure whether from within or without the abdomen or thorax pulmonary ventilation is not carried out properly. As a consequence there is a very uneven distribution of the inspired air throughout the alveoli and in consequence periodic or Cheyne-Stokes breathing results which is always a sign of

oxygen-want. These observations explain orthopnœa, as in the prone position there is an acute want of oxygen in certain pathological conditions. When the patient sits up there is a greater and more efficient expansion of the lower part of the lungs, and as a consequence many of the alveoli are ventilated with greater ease. The explanation of the periodicity of Cheyne-Stokes breathing is of great physiological and clinical importance and is a very beautiful demonstration of the control of respiratory rhythm.

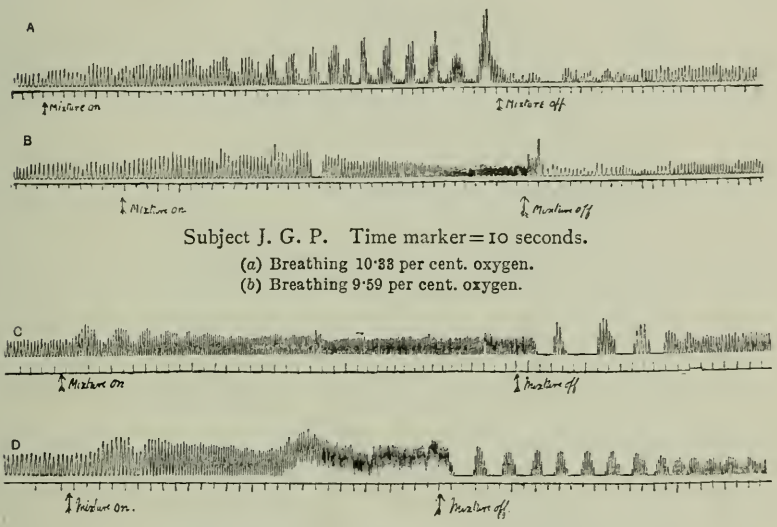
In an experiment by Haldane and Douglas a period of violent over-ventilation of the lungs removed an excessive amount of carbon dioxide from the arterial blood and the amount of oxygen in the alveoli was much increased, consequently a period of apnœa occurred. As the carbon dioxide and oxygen in the alveolar air approach normal, respiratory rhythm begins again. The oxygen is increased, the carbon dioxide diminished, apnœa ensues. When they approach the normal again respiration commences, and so this goes on until eventually the oxygen and carbon dioxide in the alveolar air reach their normal equilibrium, and so there is a return of normal respiratory rhythm. Cheyne-Stokes breathing will always be initiated when want of oxygen occurs, and at the same time carbon dioxide is suddenly eliminated from the arterial blood. In this way Cheyne-Stokes breathing is explained—when the tissues of the respiratory centre are deficient in oxygen, the amount of oxygen in the arterial blood is increased by over-ventilation, which promotes an excessive removal of carbon dioxide from the arterial blood and a period of apnœa follows with a resulting period of oxygen-want, and so the condition continues. It would be very much more frequent in normal people if it were not that there is a certain inertia in the response of the respiratory centre, so that in talking, swallowing, etc., this slight inertia allows the respiratory act to go on in an obviously regular fashion.

In acute oxygen-want, as seen in high altitudes or in mines (blackdamp or chokedamp, which is merely due to a deficiency of oxygen), the individual is suddenly overcome. In the top curve of Fig. 7 the oxygen of the inspired air is 10·3 per cent. instead of 21 per cent.

The breathing becomes more extensive in its excursion and gradually there is occurrence of a periodicity which is a definite Cheyne-Stokes breathing. On the other hand, if the oxygen be

reduced further this increased ventilation is not sufficient and suddenly the respiration centre begins to fail and the respiratory movements become very rapid and shallow. The first danger signal is the occurrence of periodic breathing of this very definite and violent type. In the lower curves of Fig. 7 there is shown another individual who does not tolerate oxygen-want so well and at 10·64 per cent. oxygen in the inspired air he shows this violent respiration becoming more and more rapid, and at the same time washing out carbon dioxide from the arterial

FIG. 7.



Subject J. G. P. Time marker = 10 seconds.
(*a*) Breathing 10·88 per cent. oxygen.
(*b*) Breathing 9·59 per cent. oxygen.

Subject J. S. H. Time marker = 10 seconds.
(*c*) Breathing 10·64 per cent. oxygen.
(*d*) Breathing 9·84 per cent. oxygen.

blood. He is suddenly allowed to fill the lungs with air, and after two or three breaths a period of apnœa ensues which remains until carbon dioxide accumulates again, and eventually normal breathing returns.

By artificially restricting the amount of air which an individual may take into the lungs at each inspiration you may induce complete suffocation; on the other hand you may reduce it to such an extent that there is not suffocation but only oxygen-want, the individual being able to get rid of carbon dioxide but not to acquire sufficient oxygen for the moment. As a consequence periodic breathing will develop. There are long periods of apnœa equal to those of hyperpnœa. On

TABLE VII.—*Quantity and Quality of Expired Air in Pneumonia.*

No.	Day of Disease.	Pulse Rate.	Temperature.	Cyanosis.	Respiration per Minute.	Volume per Respiration, c.c.	Volume per Minute in Litres.	Expired Air.			Barometric Pressure.	Result.	Remarks.
								Oxygen, per cent.	Carbon Dioxide, per cent.	Respiratory Quotient.			
1	2	100	103·6	0	38	310	11·78	18·14	2·46	0·83	758	.....	Right lower lobe involved.
	4	104	104·4	0	45	270	12·15	18·20	2·43	0·86	752		
	6	120	104·2	+	54	230	12·42	18·84	2·14	1·01	763		
	7	140	104·6	+ +	60	210	12·60	19·13	2·00	1·11	757	Died	
2	3	106	104·4	0	42	300	12·60	17·89	2·86	0·91	755	.....	Right lower and middle lobes involved.
	5	110	104·0	0	44	294	12·93	17·96	2·76	0·87	754		
	6	108	104·2	0	45	290	12·75	17·98	2·83	0·93	752		
	7	100	98·0	0	34	330	11·22	17·40	3·24	0·88	753	Crisis	
	8	80	98·4	0	24	420	10·08	17·14	3·29	0·85	757		
	9	84	98·2	0	18	505	9·09	17·04	3·58	0·86	758	Cured	
3	4	110	103·4	0	40	300	12·00	17·76	2·79	0·83	759	.....	Left upper lobe involved.
	6	108	104·1	0	42	286	11·91	17·94	2·82	0·91	756		
	7	104	104·3	0	45	270	12·15	18·01	2·84	0·94	748		
	8	110	104·4	+	52	240	12·48	18·56	2·36	0·98	755		
	8	124	102·3	+ +	54	232	12·52	18·83	2·18	1·03	766		
	9	130	103·2	+ +	64	188	12·03	19 01	2·10	1·09	762		
	9	146	101·0	+ + +	66	160	10·56	19·30	1·96	1·23	761	Died	
4	4	120	104·2	+	54	220	11·88	18·64	2·32	0·99	740	.....	Right upper and left lower lobes involved.
	5	132	104·1	+ +	52	225	11·70	18·50	2·38	0·95	748		
	6	120	104·2	+	48	230	11·40	18·41	2·45	0·94	746		
	7	110	100·0	0	40	260	10·40	17·95	2·87	0·94	754		
	8	100	98·0	0	28	350	9·80	17·33	3·06	0·81	760	Crisis	
	10	80	97·4	0	18	510	9·18	17·01	3·46	0·85	762	Cured	

enriching the small amount of air breathed with oxygen, the breathing becomes regular. This is most important in regard to pneumonia because the characteristic breathing of pneumonia is rapid and shallow, producing inefficient ventilation. The great diminution in the volume of the individual respirations in pneumonia is clearly shown in Table 7. Further the increas-

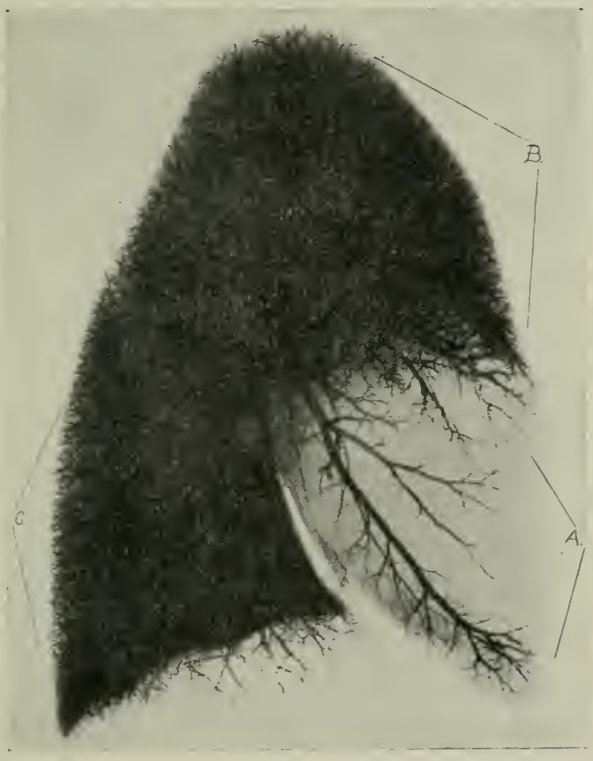


FIG. 8.

ing shallowness of the respirations is correlated to the increasing cyanosis.

This great restriction of respiration is a very serious condition of affairs, and to my mind is one of the most serious factors in lobar pneumonia, particularly where there is a very small area of lung affected, as in apical pneumonia, because the less the amount of lung out of commission the more inefficient will be the ventilation of the remaining functioning portions when the volume of each respiration is so much diminished.

It will be noted from Fig. 8 (A) that in lobar pneumonia there is practically no circulation through the lobe in grey hepatisation. As a consequence there will be no pollution of the general circulation. If blood were allowed to come through it would go back to the arterial circulation practically as venous blood and as a consequence the arterial blood would be deficient in oxygen as in congenital heart disease.

In red hepatisation (Fig. 8 (B)) you will observe that the circulation though lessened is still operative and you may have noticed that it is often in the period of red hepatisation of lobar pneumonia that the most pronounced cyanosis occurs.

Table III.

Serial No.	Day of Disease.	CO_2 c.c. vol. per cent. in 100 c.c. of Arterial Blood.	Oxygen per cent. Saturation of 100 c.c. of Arterial Blood.	Remarks.
1	5th	...	83	Some delirium.
	8th	...	82	Delirious.
	8th	...	91	On oxygen.
	9th	...	91	,, ,,
	10th	...	84	Semi-delirious. Off oxygen.
	11th	...	95	Crisis.
	15th	...	95·5	Convalescent.
2	6th	...	88·80	
3	5th	...	92·00	
4	5th	...	87·90	
5	6th	...	87·87	
6	9th	42	86·58	Slightly delirious.
7	8th	...	89·66	
8	8th	42	82·13	Delirious.
9	7th	41	80·06	Semi-comatose.
10	6th	44	91·56	
11	4th	48	93	
	5th	44	92	
	6th	46	91	
	7th	46	91	
	10th	46	90	
12	...	...	95	Before pneumonia.
	2nd	67	89	
	6th	45	84	Delirious.
	7th	47	93	On oxygen.
13	7th	42	93	
14	6th	39	80	
	8th	45	92	On oxygen.
	10th	43	92	,, ,,
	24th	54	95	Convalescent.

Gases in the arterial blood of cases of lobar pneumonia.

In Table III. will be found the arterial oxygen saturation in a series of cases of lobar pneumonia and in practically all of them

there is definite evidence of a deficiency of oxygen. In Case 12 the arterial blood was 95 per cent. saturated before the pneumonia—but during the course of the disease there was rapid oxygen desaturation of arterial blood—second day 89, sixth day 84, quite delirious—put on oxygen, and the saturation came practically to normal again with a disappearance of the delirium. There is another point of great importance shown by these cases. The normal arterial blood contains about 50 volumes per cent. of carbon dioxide. In these cases of lobar pneumonia this is distinctly low except in Case 12 (Table III.), when, during the first thirty-six hours of his illness, during the period of red hepatisation, there was definite retention of carbon dioxide, and as a consequence very violent hyperpnœa occurred which is most usually produced through an accumulation of carbon dioxide with want of oxygen.

TABLE IV.

No.	Day of Disease.	Oxygen per cent. Saturation of 100 c.c. of Arterial Blood.	CO_2 c c. vol. per cent. in 100 c c. of Arterial Blood.	Remarks.
1	6th	75	70	
	6th	98	72	On oxygen.
2	6th	85	54	
3	10th	89	...	
4		97	...	
5	9th	93·5	51	
6	10th	90	...	
	13th	86	53	
7		79	85·5	On oxygen.
		18	85·3	Not on oxygen.

Gases in the arterial blood of cases of broncho-pneumonia.

In Table IV. are shown the arterial blood gas findings in cases of broncho-pneumonia. In addition to the deficiency of oxygen in the arterial blood it is most important to note the increase of carbon dioxide in the arterial blood in these cases of broncho-pneumonia, which is quite different from the findings in lobar pneumonia. This goes far to explain the deep blue type of cyanosis so frequently found in broncho-pneumonia. This purple type of cyanosis is very striking, but at the same time it is indicative that the general circulation is being stimulated by the accumulation of carbon dioxide. Although dangerous it is not nearly so dangerous as the leaden hue or livid type,

because this indicates a vaso-motor paralysis, and oxygen-want with circulatory failure invariably leads to death unless forestalled by vigorous oxygen therapy.

TABLE V.

Case.	Diagnosis.	Hb. per cent.	Total Oxygen Capacity of 100 c.c. of Arterial Blood.	Oxygen per cent. Saturation of 100 c.c. of Arterial Blood.
			c.c.	
1	Acute Bronchitis with emphysema .	110	20·27	87 96 on O_2
2	Chronic bronchitis and emphysema .	110	20·40	89
	,, ,,	110	20·40	96 on O_2
3	,, ,,	111	20·51	90
	,, ,,	111	20·51	94 on O_2
4	,, ,,	109	20·24	90
	,, ,,	109	20·24	97 on O_2
5	,, ,,	110	20·30	86
6	Moderate emphysema . . .	110	18·6	95

Oxygen saturation of the arterial blood in cases of chronic bronchitis and emphysema.

In Table V. are shown the oxygen saturation of the arterial blood in cases of emphysema. It will be noted that there is moderate but definite desaturation of arterial blood—an increase in R.B.C. and of hæmoglobin, which is a normal response to chronic oxygen-want. Although as a consequence the blood may carry as much or more oxygen than normal, this is not as readily available, as the pressure of dissolved oxygen of the plasma is less than normal, and although the reservoir may be increased the feed pipe is diminished due to the low oxygen pressure of the plasma.

When resistance to breathing be introduced the first response is a slowing and deepening of respiration as shown in Fig. 9,

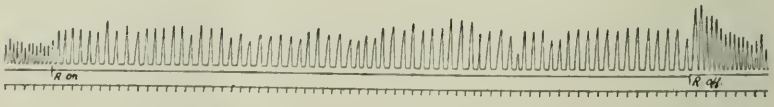


FIG. 9.—Effects of Resistance. In this and the subsequent figure inspiration = upstroke. Time marker = 10 seconds.

which is quite compatible with comfort. If the resistance be increased the response will be an increase of rate (Fig. 10), but corresponding decrease in depth until the respiration becomes jammed, which is indicative of a paralysis of the respiratory

centre through oxygen-want and accumulated carbon dioxide. Immediately the resistance is removed enormous hyperpnœa occurs and is required in order to get rid of the accumulated carbon dioxide and to allow the blood to acquire oxygen. These phenomena may be frequently observed in severe cases

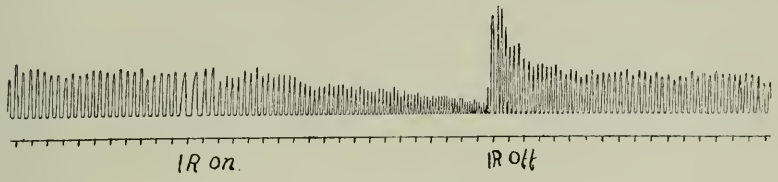


FIG. 10.—Effects of Resistance.

of spasmodic asthma. Apart from asthma they have a very practical bearing on anæsthesia. In the open manner of giving anæsthetics little or no resistance occurs. But if the inspiration and expiration are interfered with through resistance it is only a question of degree of resistance and length of time before paralysis of the respiratory centre occurs. This is particularly the case in nitrous oxide anæsthesia without oxygen added to the inspired mixture.

In certain cardiac diseases disturbances of respiration are prominent symptoms. In Table VI. are recorded a number of cases of auricular fibrillation showing varying degrees of dyspnœa and varying degrees of arterial oxygen deficiency.

TABLE VI.

No.	Heart Rate.	Oxygen per cent. Saturation of 100 c.c. of Arterial Blood.	Signs of Œdema of Lungs.	
1	75	91	+	
2	120	91	+	
3	80	96	–	
	78	89	++	
	78	97	++	Oxygen given 2 litres per minute.
	78	95	–	
4	90	95	--	
5	110	79	+++	Delirious.
	108	98	+++	Oxygen given 4 litres per minute Delirium disappeared.

Oxygen saturation of the arterial blood in cases of auricular fibrillation.

These findings are not apparently due to disturbance of the cardiac rate but rather depend upon the presence of œdema of the lungs. In valvular lesions such as mitral stenosis there is

a very pronounced deficiency in the quantity of blood which goes to the tissues per minute—instead of 5 to 7 litres it may be but 2 to 2½ litres. During periods of rest the tissues are obtaining barely a sufficient quantity. On account of the structural changes the heart is incapable of adequately increasing the quantity of blood to the tissues on exercise, therefore violent dyspnœa, palpitation, and cerebral symptoms such as giddiness, vertigo, etc., soon develop. If there be present a slight degree of œdema of the lungs with lowered saturation of the arterial blood with oxygen it will be quite obvious how all these symptoms may be exaggerated even at rest.

Respiratory Failure.—There are two distinct types of respiratory failure. One associated with low carbon dioxide in the blood with or without primary oxygen-want as demonstrated by the experiments of Henderson and Haggard, and of Dale and Evans. In this type there is an acute respiratory and vaso-motor failure and it may be termed the acapnœic type. Secondly, there is the other type where oxygen-want is associated with carbon dioxide retention. The latter keeps up the vascular tone but soon wears out the respiratory centre. These cases usually show deep blue cyanosis in distinction to the livid cyanosis of the first type. This second type may be termed the asphyxial type of respiratory failure.

How is oxygen-want to be treated? In pneumonia with cyanosis there is a clear indication for the administration of oxygen, and it is most important that it should be given early. I am certain more cases would recover if the cyanosis were not allowed to develop, or if it has developed if it were removed immediately by effective oxygen administration. In all pulmonary lesions, such as lobar pneumonia, broncho-pneumonia, capillary bronchitis, œdema of the lungs, suffocative gas poisoning, etc., where there is cyanosis, the proper administration of oxygen is imperatively indicated. By increasing the concentration of oxygen in the inspired air the amount and partial pressure of oxygen in the alveolar air will be increased, and thus the passage of the gas into the arterial blood will be greatly facilitated.

In cardiac or vascular disease where the lungs are healthy, the administration of oxygen will not avail, as here it is not a question of increasing the oxygen saturation of the arterial blood, which is already fully saturated, but rather of adopting

means of increasing the amount of blood reaching the tissues by increasing the efficiency of the cardiac action or of making the smaller arteries more permeable to the blood stream. Where œdema or passive congestion of the lungs be present, as indicated by crepitations through the lower lobes, then oxygen therapy is definitely indicated for reasons already mentioned.

Good results from oxygen therapy may only be expected if it be given properly. The discussion of this question I will leave for Dr Davies to lay before you.

METHODS FOR THE THERAPEUTIC ADMINISTRATION OF OXYGEN.

By H. WHITRIDGE DAVIES, M.B., B.S.

Preliminary Considerations.—In the foregoing communication Prof. Meakins has pointed out the necessity for oxygen administration under various conditions. It remains to consider the means whereby oxygen may be given most effectively and economically. The traditional method of oxygen administration by means of a rubber tube and glass funnel represents the extreme of waste and inefficiency and is about as effective and rational as it would be to spray tincture of digitalis about the room in a case of auricular fibrillation. Oxygen therapy has fallen into disrepute mainly on account of such faulty methods, also on account of the fact that it has been applied in conditions where physiological investigation has shown that it can be of no possible use, and further it is usually reserved as a last resort and applied in cases where the respiratory and circulatory failure have progressed to such a degree that the patient is moribund. It is firmly established that in conditions of oxygen-want not due to impairment of the circulation or to direct poisoning of the tissues, oxygen is a valuable remedy when administered early and effectively.

Oxygen must be regarded as a drug, and its dose regulated according to the needs of the patient. Moreover the fact that, like other valuable drugs, it may, if given in great excess, produce toxic symptoms, does not limit its usefulness provided it be given by efficient means and in proper dosage. Occasionally, as pointed out by Haldane, when oxygen is given to a

patient comatose or semi-comatose from oxygen-want, the improvement in the patient's general condition may cause subjective symptoms to become more marked. This should not be taken as an indication that oxygen administration has failed and must be discontinued, but rather, on the other hand, as evidence of definite improvement.

An adult man with the increased metabolic rate of fever may breathe up to 10 litres of air per minute. Atmospheric air contains approximately one-fifth of its volume of oxygen, so that if the individual breathes at the rate of 10 litres per minute the addition of 2 litres of oxygen per minute to the inspired air will practically double its oxygen percentage, and therefore its partial pressure of oxygen. Clinically one finds that more than this amount is seldom necessary and frequently less may be sufficient. The ideal method of regulating the dosage is to find the minimum amount necessary in order to restore the arterial oxygen saturation to normal. This involves methods of blood-gas analysis which are seldom available, but fortunately it has been shown by Prof. Meakins and others that clinical evidence, namely the relief of cyanosis, delirium, and restlessness, are coincident with the restoration to normal of the arterial oxygen saturation. The beneficial effects of oxygen are seen to the best advantage in cases of pneumonia of moderate severity. A patient slightly cyanosed, with restlessness and low muttering delirium, improves as by magic—cyanosis disappears, and the patient, especially at night-time, often falls into a quiet, restful sleep which not infrequently marks the beginning of convalescence.

A further point in regard to oxygen administration is that it must be continuous. The lungs, blood, and tissues possess no storage capacity for oxygen and are entirely dependent for their needs on the supply available from moment to moment. Many cases however of slight, one might almost say potential, oxygen-want do not require oxygen during the daytime when propped up in bed. At night-time, however, when the patient falls off to sleep he may slip down in bed, and the resulting change from the orthopnœic position causes a potential oxygen-want to become an actual one. Sleep becomes disturbed by terrifying dreams which often cause the patient to wake up. The best remedy in conditions of this sort is continuous oxygen at night-time, and on this account oxygen may almost be regarded as a hypnotic.

The Oxygen Chamber.—The oxygen chamber is the ideal method for administration of oxygen. By this means it is possible to regulate the percentages and partial pressures of gases in the inspired air to any required degree. The size of the chamber may vary from that necessary for a single bed to that for several. Large chambers for the accommodation of several patients have been used at Cambridge, Stoke-on-Trent, and Guy's Hospital, and encouraging results have been reported. The essentials for an oxygen chamber are as follows :—

(1) The chamber must be moderately if not absolutely gas-tight.

(2) There must be an arrangement for the analysis of samples of air from the chamber from time to time.

(3) The air must be purified of carbon dioxide, water vapour, and organic impurities, either by means of large trays containing soda-lime, calcium chloride, and solution of potassium permanganate, or by an external purifying circuit.

(4) Substances which only smoulder or burn very slowly in ordinary air become highly inflammable when the oxygen percentage is increased. Hence no lights of any kind or electric wiring can be allowed inside the chamber. As an additional precaution the chamber itself and its contents should as far as possible be rendered non-inflammable, and further there should be in close proximity means for extinguishing fires.

(5) Oxygen must be added from time to time in order to maintain the oxygen of the chamber at the required percentage.

(6) The chamber should be provided with an air lock in order to permit the entrance and exit of nurses, physician, and others with a minimum of loss of oxygen.

The difference between the oxygen of the inspired and expired air is seldom more than 5 per cent., representing an oxygen *consumption* at the very most of half a litre per minute. This amount, together with a little more to allow for leaks and loss of oxygen by other means, should be amply sufficient to maintain the oxygen of the chamber at the required percentage. A small single-patient chamber of about 200 cubic feet capacity, if filled with air, would contain about 40 cubic feet of oxygen, so that in order to double the oxygen percentage about 50 cubic feet of oxygen should be added from a cylinder. A small portable collapsible oxygen chamber for a single patient has recently been placed on the market by Messrs Siebe

Gorman & Co., Ltd., of London. The same firm also make and supply the still simpler oxygen bed-tent of Prof. Leonard Hill, F.R.S., which covers only the head and thorax of the patient.

The Haldane Oxygen Administration Apparatus.—This apparatus, already familiar to many, was devised for, and used with great success in, the treatment of gassed cases during the war. It consists of a screw adaptable to the heads of standard oxygen cylinders, a pressure gauge to show the amount of oxygen in the cylinder, a reducing valve to reduce the pressure of oxygen to two atmospheres, and a graduated regulating valve. The light field pattern apparatus was designed to deliver 0 to 4 litres per minute, while the larger later type delivers up to 10 litres per minute. This portion of the apparatus is connected to the face-piece by means of a rubber tube of suitable length. The face-piece consists of a metal mask, with pneumatic-rubber cushion and with two valves, one to allow inspiration of as much atmospheric air as may be necessary, the other to conserve oxygen by directing the stream into a small reservoir bag during expiration. It is generally agreed among those who have had much experience of this apparatus that in circumstances where an oxygen chamber is not available it forms the most efficient, convenient, and economical method for oxygen administration. No special skill is required in its use, and the apparatus can be left on the patient for several hours without supervision. The patient, as a rule, experiences no discomfort from the mask, and can usually sleep comfortably with it on. There are, however, a few cases where the mask is strongly resented, and as a rule these cases are of the asphyxial type of respiratory failure where oxygen-want is associated with carbonic acid retention and consequent severe dyspnœa. In cases of this type some other means must be used.

Some of the older outfits of this type have been found after a year or so of use to become defective both in the reducing and regulating valves—hence it may be necessary to set the regulating valve at a higher figure in order to deliver sufficient oxygen to produce clinical signs of improvement. Should there be reason to suspect such defects it is advisable to have the apparatus tested against a meter, and if the flow be not accurate the apparatus should be returned to the makers for repair. Grease or oil in any form should not be applied to this

apparatus, owing to the well-known fact that such substances in the presence of oxygen are liable to spontaneous combustion. The apparatus is manufactured and supplied by Messrs Siebe Gorman & Co., Ltd., of London.

The Nasal Catheter Method.—This method consists in passing a continuous slow stream of oxygen into the naso-pharynx by means of a soft rubber catheter or other suitable appliance. Apart from its wastefulness, at least half of the oxygen being lost with the expired air, this method is effective and particularly useful in children and in those cases where

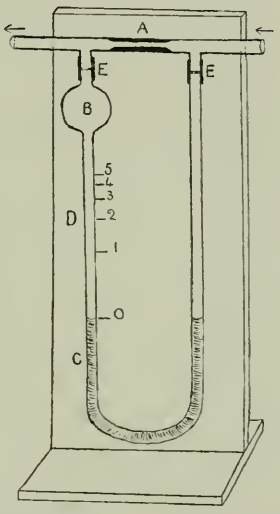


FIG. I.—A SIMPLE TYPE OF FLOW METER.

A. Constriction—2 mm. diameter.
B. Glass bulb to retain fluid in case gas is turned on too suddenly.
C. Water coloured with ink or methylene blue.
D. Graduations—litres per minute.
E, E. Rubber joints.

The direction of flow of gas is indicated by arrows.

a mask cannot be tolerated. The catheter is introduced along the floor of the nose and then fixed in position by means of a small strip of adhesive plaster applied to the face. It is necessary to have some type of flow metre in order to gauge the amount of oxygen delivered, and as at least half the oxygen is lost during expiration it is necessary to give at least twice as much oxygen as one would give by means of the Haldane apparatus. Thus when oxygen is administered by means of the nasal catheter at least 3 to 4 litres per minute are required

to increase adequately the oxygen percentage of the alveolar air in a case with average pulmonary ventilation. A very rough-and-ready method of gauging the flow is that of bubbling the oxygen through a wash-bottle in a steady, continuous stream. Single bubbles, even at the rate of two a second, would represent a flow of less than a tenth of a litre per minute and would thus be entirely inadequate. A simple type of flow meter is shown in Fig. I. This apparatus can be made by any glass blower or laboratory mechanic in a few minutes and is calibrated against a metre, or by passing gas at known rates of flow by means of the Haldane apparatus. The gas must not, however, be turned on suddenly, otherwise the liquid in the gauge will be forced up through the outlet.

Emergency Methods.—Should none of the above methods be available, various emergency methods can be used. The tube and funnel method, though very wasteful, can be made efficient by using a rapid stream of oxygen and holding the funnel within an inch or two of the patient's face. Oxygen may also be given very effectively and in a pure form by means of a nitrous oxide administration bag.

Mackenzie has described a means whereby the patient's head is enclosed in a cardboard hat-box of suitable size, a suitable opening being cut for the neck, and the stream of oxygen being directed into the box. Five to ten litres per minute would be necessary with this method.

Summary and Conclusions.—(1) The immediate object to be attained in oxygen therapy is to increase the percentage and therefore the partial pressure of oxygen in the alveolar air. Thus oxygen is given a more powerful *vis a tergo* in its passage through damaged, altered, or thickened alveolar epithelium into the blood.

(2) The absolute amount of oxygen required to effect this object depends upon the rate of pulmonary ventilation of the patient and on the means whereby the oxygen is administered.

(3) The attainment of this object is indicated by the return to normal of the oxygen saturation of the arterial blood and the coincident relief of clinical signs indicative of oxygen-want of the *tissues*, namely cyanosis, delirium, and restlessness.

(4) The methods of oxygen administration in order of their efficiency are firstly the oxygen chamber, secondly the Haldane apparatus, thirdly the nasal catheter, and lastly the various emergency methods described above.

(5) Administration of oxygen subcutaneously, intraperitoneally, or by similar means is neither justified nor necessary.

Discussion.

The President (*Sir Robert Philip*) thanked Professor Meakins for his valuable contribution. The crisp and clear précis of the address given in the Society's billet—a model of what such a précis should be—had awakened much interest, and that interest had been amply satisfied by the illuminating demonstration to which they had listened. The object-lesson given by Dr Whitridge Davies had further enhanced its value. The address presented many aspects of extreme interest—physiological and pathological—and was rich in suggestion.

Dr W. T. Ritchie said that the communication given by Professor Meakins touched on many problems of great interest and importance, and afforded an explanation, based on experimental research, of some obscure clinical phenomena. Twenty years ago oxygen was considered to be of great value in the treatment of pneumonia, despite the criticism of physiologists. The pendulum had now swung in the other direction, and experimental physiology was establishing the value of oxygen therapy on a sound basis. Nature's methods of adaptation and compensation in disease were well exemplified in the polycythæmia associated with cardiac failure to which attention was directed by Dr George A. Gibson in 1903. The artificial production of Cheyne-Stokes breathing in healthy individuals and its arrest by oxygen, went far to explain many of the phenomena associated with this form of breathing in disease. In artificially produced Cheyne-Stokes breathing, however, the volume of the respirations during each dyspnœic phase did not appear to wax and wane as in the Cheyne-Stokes breathing accompanying disease.

Dr Guy said that he had been most interested in the part of Professor Meakin's paper which dealt with the question of anæsthetics. He stated that in England it was still the general practice to administer nitrous-oxide gas through valves, thus producing a mixed anæsthesia and asphyxia. In his opinion this was a scandal; nitrous-oxide gas should never be administered except in combination with oxygen, since the combined gases caused the minimum interference with the rhythm and rate of respiration. Furthermore the asphyxial element which accompanied the administration of nitrous-oxide gas alone was eliminated. Another interesting deduction was that the posture employed for the patient, *i.e.*, the sitting posture, in all probability was the one which was most suitable and fraught with the least danger.

Dr J. H. Gibbs emphasised the importance of avoiding any asphyxial element in the administration of anæsthetics. Nevertheless it was sometimes impossible to avoid a certain amount of cyanosis

owing to spasm in the early stages of induction, and as it was of short duration, it was of no consequence.

Dr Goodall said that he had been much interested in the curve showing the hæmoglobin-oxygen combination in a case of cyanosis. The patient was cyanosed because her blood took up too little oxygen, but other symptoms were absent because the blood parted with oxygen to the tissues with unusual facility. Such a case indicated that mere oxygen content and hæmoglobin percentages were not the only factors in the problem. A good example of this was seen in comparing a case of pernicious anæmia with one of secondary anæmia, each with, say, 40 per cent. of hæmoglobin. The secondary anæmia case was by far the most distressed of the two. Cases of pernicious anæmia showed great variations from time to time as regards breathlessness while maintaining the same percentage of hæmoglobin.

Professor Meakins in reply agreed with Dr Ritchie that there were certain difficulties in exactly reproducing abnormal conditions in a normal person. The periodic breathing of arterial disease or cerebral pressure depended on the circulation rate and blood pressure as well as on the pulmonary ventilation, and as a consequence there was an inertia on the respiratory centre which made the periods of hypernœa and apnœa longer but in principle practically the same. In regard to anæsthetics he agreed with the views expressed by Dr Guy, but he did not know that nitrous oxide was ever administered now without oxygen in combination. It had a definite action on the central nervous system, but given without oxygen it was nothing more than asphyxiation. With regard to the administration of ether he said that there was nothing against its being administered by the open method, but the ideal method of giving any anæsthetic was to be sure that the patient had a sufficiency of oxygen. With regard to his remarks about the unique patient quoted and referred to by Dr Goodall, her case was given to show that a patient could be cyanosed and yet have no discomfort. The question of anæmias was, he said, of great interest but had been omitted owing to the lateness of the hour.

PRIVATE BUSINESS.

Meeting—7th June 1922.

John Barré de Winton Molony, O.B.E., M.B., Ch.B., F.R.C.S.E., and John James M'Intosh Shaw, M.D., F.R.C.S.E., were elected Members of the Society.

Meeting—5th July 1922.

Douglas Miller, M.B., F.R.C.S.E., was elected a Member of the Society.

THE CHOICE OF METHODS EMPLOYED IN THE SURGICAL DIAGNOSIS OF RENAL DISEASE.*

By HENRY WADE.

THERE are some who believe that the future of medicine resides in the more accurate recognition of the earliest manifestations of disease. By none will those discoveries be more cordially welcomed than by members of the surgical profession, who have for long realised that successful surgery was largely dependent on early diagnosis and early radical treatment of the diseases that fall within their province.

In seeking for the earliest manifestations of disease there would appear to be two Schools of thought—those who rely mainly on the subjective sensations of the patient, such as the incidence of pain, its nature and distribution; and those who pin their faith to the detection by physical means of some departure from the anatomical standard of structure or contour of the healthy human body, or alteration in its normal physiological mechanism. The former I would call the Idealists, and the latter, of whom I would claim to be one, the Materialists of medicine.

Failure in the surgical diagnosis of renal disease is usually due to an omission to employ the most appropriate method for its recognition. These methods are, however, now so numerous and certain of them not devoid of danger that it is essential to make a judicious selection of the most suitable, based on the clinical findings of the case.

The difficulties of detecting a needle in a hay-stack are entirely dependent on the method employed. The solution of the problem is comparatively simple, if you will provide the necessary X-ray equipment and a Mackenzie-Davidson localiser. The problem before us this evening, succinctly, is this—when must we X-ray the hay-stack and how can it best be done?

The first question that arises is, what are the subjective symptoms or gross physical signs which warrant a detailed investigation of the genito-urinary system being carried out?

I do not wish to belittle the value of the patient's narrative in many cases, nor do I wish to cast doubts upon the value of

* Read 5th July 1922.

that most valuable, but almost indefinable aid to diagnosis, the clinical instinct of the able physician, but at the same time I think it must be conceded that their greatest value is in carrying us to the threshold of discovery, the exact and accurate final diagnosis being largely achieved by instrumental aid.

(1) The popular symptom of renal disease is *pain in the loins.* "Every picture tells a story": frequently the narrative is a renal romance due to lumbago. It may, however, be renal in origin and due to renal residual urine retention producing pelvic distension.

(2) *Renal colic.*—This classic and characteristic agony is due to intermittent obstruction of the ureter and usually owes its origin to the presence of a calculus within the lumen, but occasionally may result from obstruction from without.

(3) *Frequency of micturition.*—It is noteworthy how often this is considered an indication only of vesical disease, whereas in many cases it is extra-vesical in origin and due to ureteral or prostatic disease.

(4) *Pus or blood in the urine* obviously indicate disease of the genito-urinary tract. In the case of the former, however, it is well to remember that although an abundant purulent discharge may be present, the urine may be sterile.

(5) *Bacilluria* or the presence of organisms in the urine is frequently a reason advanced for a detailed examination of the genito-urinary tract. Such is always justified, as by this means it is frequently found to be due to a chronic pyelitis. At the same time, it must be remembered that many such cases are eliminative in origin and arise from a primary lesion in the bowel or elsewhere.

(6) *The palpable kidney.*—When this is *bilateral* it is most commonly part of a general visceroptosis, a secondary consequence of a more generalised disease and seldom calls for detailed local investigation or local treatment. When both kidneys are palpable and there is no general visceroptosis, we very strongly suspect the presence of congenital multiple cystic disease and in those cases most careful further investigation is indicated. When the condition is *unilateral* and only one kidney is palpable, there is usually disease of the renal organ. At the same time, it must be remembered that in a patient with renal disease, the diseased kidney may not be palpable and the healthy one palpable, for the kidney that has undergone compensatory hypertrophy can usually be felt.

When a detailed examination is warranted, what procedure is recommended to be followed?

Is it ever permissible to operate forthwith without further investigation? Such a course is justified where the kidney has been accidentally ruptured and serious hæmorrhage has resulted. It is also recommended where acute fulminating suppurative pyelonephritis seriously endangering the patient's life is present. In both cases, however, the functional activity of the opposite kidney must be investigated and the best course is to open the peritoneal cavity at the time of the operation, and by passing the hand across the abdomen examine the state of the healthy organ.

I will next rapidly review the routine examination carried out in all renal cases.

The usual *clinical examination* is of course made. Thereafter the urine is examined. A twenty-four hours' sample is collected in a large vessel, 5 c.c. of toluol being added to prevent decomposition. The percentage of the usual normal constituents, such as urea, is estimated, and any abnormal content examined for. Thereafter a freshly voided sample of morning urine is obtained, collected in a specimen bottle that can be easily sterilised and is sealed like a milk flask. The name and particulars of the patient are recorded on the sterilised cardboard stopper. From an immediate cytological and hasty bacteriological examination of this specimen much can be learned. If pus cells or organisms are present in a film made from the centrifuged deposit, it can safely be assumed that they are from the genito-urinary tract.

Next comes the *preliminary X-ray examination*, which includes the kidneys, ureter and bladder, and the photograph of the last should be taken with the direction of the rays at right angles to the plane of the pelvic brim, so as to reveal the bladder floor and ureteral orifices. Elaborate preparation of the bowel for this examination is in my opinion not necessary. I would not emphasise the necessity of this preliminary X-ray examination if it were not for the fact of my having had recently under my care two cases, both patients who had been treated for several years for persistent cystitis without relief and both having been cystoscoped without an X-ray examination. Dr Hope Fowler's photographs of these cases showed in each a kidney destroyed by caseous tubercle.

Finally, comes the usual simple *cystoscopic examination.*

This can best be done in the great majority of cases without a general anæsthetic, and for some time now I have dispensed with a local anæsthetic. In the female patient, it should never cause pain, but naturally often creates much mental distress, to mitigate which two things are necessary—suitable environment for the examination, and a nurse experienced in the preliminary arranging and preparation of the patient. If pain is caused in a male patient, it is not an indication for a general anæsthetic, but for the use of a smaller cystoscope.

On the findings revealed by this routine examination the necessity for further investigation will be determined, and that will probably be conducted to determine—(1) the source of suspected renal hæmorrhage; (2) the source of pus in the urine; (3) the nature of a suspicious shadow revealed by the X-ray examination; (4) the explanation of an apparent increase in the size of the kidney; (5) whether an abnormal swelling felt within the abdomen is a displaced kidney; (6) whether vague discomforts in the loin are renal in origin.

To achieve success in these endeavours, the methods at our disposal are (1) chromocystoscopy; (2) ureteral catheterisation; (3) estimation of pelvic capacity by renal lavage; (4) passage of an X-ray catheter which is photographed *in situ;* (5) pyelography; (6) a detailed cytological and bacteriological examination of the urine with the injection of a guinea-pig if necessary; (7) blood analysis.

(1) Investigation of the cause of *suspected renal hæmorrhage.*—In a case of intermittent hæmorrhage, it is a sound policy to wait and examine at the time when bleeding is taking place. If this is not possible and no vesical cause such as a villous papilloma or trigonitis is seen on cystoscopic examination, what assistance does the ureteral catheter provide? Not so much as some imagine. The vascular mucous membrane of the ureter and renal pelvis bleed readily, even when a soft catheter is gently introduced. A trace of blood often appears after the catheter has been inserted for ten minutes, owing to the irritation of its presence. If, however, urine tinged with blood appears immediately on introducing the catheter into the renal pelvis it can safely be assumed that the hæmorrhage is due to a pathological lesion and is most likely produced by chronic pyelitis. If the introduction of the catheter into the pelvis is followed by the sudden escape of bright blood, which soon stops when a clot forms inside the catheter, the likeliest

explanation is the presence of a vascular tumour, such as a hypernephroma invading the renal pelvis.

Confirmatory evidence of the presence of chronic pyelitis is usually obtained by estimating the capacity of the renal pelvis. This is done by renal lavage. A 10 c.c. syringe containing sterile boric lotion is attached to the catheter and the fluid very gently introduced. The patient is told to mention at once when any discomfort is felt. The healthy renal pelvis has a capacity of from 5 to 7 c.c., and in the normal pelvis when this amount of fluid has been introduced the patient at once complains of a sharp pain in the loin.

When slight hydronephrosis is present, as is always the case where chronic pyelitis exists, 15, 20, or 30 c.c. may be introduced before discomfort is complained of.

To confirm the diagnosis of the presence of a renal neoplasm, a pyelogram must be taken. The technique is very similar to that of real lavage, except that the fluid introduced is 15 or 20 per cent. sterile sodium bromide. As soon as the pelvis and calyces are distended the photograph is taken. In doing so, naturally the more rapid the exposure the better the result. The photograph or pyelogram will reveal the diagnostic signs of tumour growth in the drawing out of the calyces and the pelvis in the direction of the tumour and later their destruction. The value of this sign is very great, and by its employment one can confidently anticipate being able to accomplish the recognition of cases of tumours of the kidney at a much earlier stage than has previously been possible.

(2) *The source of pus in the urine.*—If both ureters be catheterised and samples of urine obtained from both kidneys, it is an extremely simple proceeding to determine which kidney is infected. I have followed this practice for many years and have found it simple to carry out and most satisfactory in the results obtained.

You may have observed, however, in a recent article by Frank Kidd that he holds strongly the opinion that bilateral ureteral catheterisation is not to be recommended. Emanating from such a source, this opinion merits careful consideration. Personally, I hold different views based on my own experience. I must certainly have carried out a bilateral ureteral catheterisation on over a thousand patients, and I do not know of one case where any serious complication followed this. In doing it, however, there are certain rules I have always followed.

It is never done on an out-patient, nor on a patient allowed to go home immediately after the examination. In all cases, the patient comes to the theatre with the kidneys functionating actively, having recently taken two pints of weak tea. After the examination, the patient is transported to bed, where he is given another warm drink and 10 grains of urotropine. If this practice is followed, I have no hesitation is saying that bilateral ureteral catheterisation may be safely practised.

(3) The *nature of a suspicious shadow* revealed by the X-ray examination.

Not infrequently there arises the problem of determining whether a shadow situated in the region of the kidney is due to a renal calculus or an extra-renal concretion, such as a calcified tuberculous gland. Sometimes two or three shadows may be in close proximity. The presence in the urine of one or two red-blood cells or pus and catarrhal cells is presumptive evidence in favour of renal calculi. The diagnosis of course is not established, especially as there is no means I know of whereby the urine from each kidney can be collected without the possibility of causing one or two red-blood cells to appear in the excretion from that side. It is also of great importance to remember that calculi may be present in the kidney or ureter, cause only a sensation of vague and indefinite discomfort and lead to the presence of no red-blood cells in the sample of urine from that kidney, or interfere with its functional activity.

A case that illustrated this point very well was one I had the privilege of examining for Sir Harold Stiles. The following are the notes concerning the patient.

"The patient is 48 years of age and has led an active life. He at present suffers from vague pains and uneasiness in the left loin. These commenced about ten years ago and have recurred at intervals since. The pain is of a dull aching character, which remains local and does not appear to have the character of renal colic. It is associated with no frequency of micturition, nor has there been at any time the presence of blood in the urine. Careful physical examination reveals no evidence of disease. Neither kidney is palpable. An X-ray examination was carried out recently by Dr Hope Fowler and it shows the presence of three oval shadows in the region of the pelvis of the left kidney. The nature of these is uncertain.

A cystoscopic examination was carried out which at first was associated with a certain degree of discomfort. Ultimately, this passed off. The bladder capacity was found to be normal. The

bladder walls were healthy. Both ureteral openings observed to be of normal appearance. Ureteral catheters passed without producing any appreciable discomfort and without meeting with any obstruction up into both renal pelves. No renal residual urine from either pelvis. An abundant flow of urine of natural appearance obtained from both kidneys. Two samples from each kidney and one from bladder collected and handed to Dr Logan for bacteriological report.

Report by Dr Logan on Specimen of Urine from Bladder and Right and Left Ureters.

Bladder specimen showed fair numbers of red-blood cells, a few polymorphs, some epithelial cells and oxalate crystals. The polymorphs are probably not more numerous than can be accounted for by the presence of blood.

Right ureter—red-blood cells, epithelial cells and some aggregations of cells without nuclei, like mulberries in appearance: some brown unorganised debris.

Left ureter—practically no red-blood cells, but very numerous epithelial cells of different types and also some pseudocasts (not true casts); some brown unorganised debris.

As Dr Hope Fowler was not available owing to illness, arrangements for a pyelogram being taken could not be made.

The patient returned home on the evening of the examination in satisfactory health.

The results of this examination were inconclusive, and as the vague pains and uneasiness in the left loin still persisted he was operated on by Sir Harold Stiles. Several renal calculi were discovered in the left kidney and were removed.

In reviewing the examination of this case, it will be observed that estimation of the renal capacity was omitted. If it had been carried out it would undoubtedly have shown dilatation of the renal pelvis to be present and provided further confirmatory evidence in favour of a lesion of that kidney. If, in addition to this, a pyelogram had been obtained, it would have confirmed the diagnosis of renal calculi by the incorporation of the original shadows revealed within the shadow produced by the opaque fluid introduced into the renal pelvis.

The illustration (shown) demonstrates this last point well. It is a pyelogram of a normal renal pelvis and ureter with an abnormal shadow beneath the lowest calyx. It is from a young girl who suffered from tuberculous disease. The

abnormal shadow was considered to be due in all likelihood to the presence of a tuberculous lymphatic gland. The kidney was exposed by operation, as early cortical tuberculous disease was suspected. At the operation a minute focus of early tuberculous disease was found and the shadow was observed to be due to enlarged tuberculous glands behind the kidney.

Where doubtful shadows are observed in the course of the ureter, these may be due to ureteral calculi. The commonest source of error on the right side is calcified tuberculous mesenteric glands. Next in frequency comes phleboliths in the ovarian or spermatic vein, which runs parallel and in close proximity to the ureter.

I will briefly describe a most interesting case illustrating the former. It is from the Clinique of Mr Miles. The patient was a young boy who had suffered from repeated attacks of renal colic. The X-ray photograph showed what appeared to be a typical shadow of a ureteral calculus. There were, however, no red blood cells in the urine. I remember his case well, as during the clinical examination for the Fellowship of the Royal College of Surgeons held last summer I was engaged with a candidate at the next bed to this patient. While thus occupied the boy developed a typical attack of renal colic. He rolled on his side, obviously suffering great pain. He became pale, was sick and vomited, and the muscles on that side became very rigid. His condition was so urgent we interrupted the examination to obtain relief for the boy. Mr Miles was so kind as to entrust me with the care of this patient. As the case was so typical and the shadow was distinct and at that time I did not possess the necessary instrument to catheterise the ureter of a young boy without a general anæsthetic, we operated without further investigation. The ureter was exposed in the usual way. It was found to be slightly dilated at its upper part, but on palpation it contained no stone. We therefore opened the peritoneal cavity in front of it and found that a calcified tuberculous gland was adherent firmly to its anterior aspect. This was dissected free and removed and the patient made an excellent recovery.

The interest of this case is not only the error in exact diagnosis with which it was associated, but also in being able to prove the presence of a stricture of the ureter of extra-ureteric origin. According to Hunner, this state of affairs is of comparatively frequent occurrence and he has published records of a thousand cases where he has met with this and treated it by dilating the ureter.

The means of differential diagnosis in cases of suspected

ureteric calculi is by the use of the X-ray catheter. The tip of the catheter is stopped virtually in all cases by the foreign body and the subsequent X-ray photograph shows it in contact with it.

My efforts to obtain information of value with the use of the wax-tip catheter have not been attended with appreciable success.

Where doubtful shadows are observed in the pelvis, these are most usually due to the presence of phleboliths. They can in the great majority of cases be recognised from their structure, contour, and situation. They have a uniform density, a smooth contour, and although they may be found in any situation are most commonly met with grouped around the ischial spine to the outer side of the course of the ureter.

(4) *The explanation of apparent increase in the size of the kidney.*—A kidney may become enlarged from many causes. When due to hydronephrosis, pyonephrosis, or such like conditions, the diagnosis is simple. . The ureteral catheter, which usually enters the renal pelvis without difficulty, at once reveals the state of affairs present in the escape of an unusually large amount of renal residual urine, probably purulent. Estimation of the capacity of the renal pelvis at once shows it to be much dilated.

When due to tumour or a large solitary cyst the diagnosis is more difficult and we have here always the possibility of the enlargement being due to compensatory hypertrophy in a case of a single functionating kidney. It is therefore essential to determine forthwith, as it always is before any operative interference is contemplated, whether the patient has one or two functionating renal organs. This subject is of more than merely academic interest. Probably about one person in 120 has a single functionating kidney.

Congenital absence or extreme congenital atrophy of one kidney is considered by some surgeons to be very rare. Morris found only three such cases in 15,904 post-mortem examinations. In 500 post-mortem examinations conducted by myself in the Royal Infirmary, I met with the condition five times. A year ago being interested in a case of acute pyelitis that had terminated fatally, I attended the pathological department of the Simpson Memorial Hospital and found Dr Rutherford concluding the post-mortem examination of another case. The finding in it that appealed to me of most interest was that

here again we had unexpectedly revealed a single functionating kidney. He then informed me that out of about 300 post-mortem examinations conducted by himself he had observed this condition twice previously. A few months ago a patient under my care in the Royal Infirmary, who suffered from advanced carcinoma of bladder, died. The post-mortem examination was conducted by Dr Alexander and again only one kidney was found, the other organ being entirely absent. This was Dr Alexander's third experience of this nature in some 400 post-mortem examinations.

The simplest and safest method of demonstrating that only one kidney is functionating is by chromocystoscopy. Cystoscopy alone is not enough, as a kidney congenitally destroyed may possess a ureter which will admit a size 5 French catheter.

The technique of this examination is well known and very simple. Four c.c. of a saturated solution of indigo carmine is injected intramuscularly into the patient, who for preference is not under a general anæsthetic and has recently imbibed a large quantity of fluid. In seven to ten minutes the pigmented urine is observed to be propelled from the ureter into the bladder from the excreting kidney.

Much can be learned from this method of examination. As a means of estimating diminished functional activity in one organ, it is not of so great value as other methods. It is, however, of great value in determining the degree of obstruction produced in a ureter by an impacted ureteral calculus. In such a case the pigmented urine is observed to be jetted forth in a vigorous manner from the healthy ureter. Where a ureteral calculus is producing partial obstruction, the pigmented urine escapes like smoke from a slow-burning fire.

Where renal enlargement is due to an hydatid cyst, the exact diagnosis is naturally difficult. It was not so, however, in the case from which this specimen (shown) was obtained. His narrative lucidly established the diagnosis. He came from Shetland, kept dogs, and complained of passing grape skins in his urine.

The kidney was much enlarged, and on ureteral catheterisation its functioned activity was only a third of that of the healthy side.

(5) *Determination whether an abnormal swelling within the abdomen is renal in origin.*—The commonest of these are the congenitally displaced kidney, especially the pelvic kidney, and

the horse-shoe kidney. The best method of settling this point is by means of a pyelogram. If the swelling in the bony pelvis is revealed by pyelography to have a pelvis and calyces, it is of course a kidney. If the swelling be due to a horse-shoe kidney, the only certain way to demonstrate this is by pyelography again. Here is such a case from Sir Harold Stiles' Clinic. You will observe a double pyelogram has been taken and it shows the diagnostic feature of a horse-shoe kidney in the direction inwards of the lower calyces which in all other conditions pass laterally from the pelvis, never medially.

(6) *Whether vague discomforts in the loin are renal in origin.* — When such exist without the preliminary X-ray examination revealing any abnormality and the urine is healthy, diagnosis is difficult. If, in addition, as is sometimes the case with a military pensioner, other influences cloud the clinical picture, it is still more so. Recently I had one such case under my care in Craigleith Hospital. On ureteral catheterisation both renal pelves were readily entered and normal urine came from both sides. On testing the pelvic capacity, however, whereas on the left or healthy side a sharp pain was produced when 7 c.c. were injected, on the other side 30 c.c. were contained before discomfort was felt. The ease with which the renal pelvis was entered being against stricture of the uretero-pelvic junction, an abnormal artery to the lower pole was suspected and this was confirmed at operation to be the cause of a slight hydronephrosis.

The value of a detailed cytological and bacteriological examination of the urine is too large a subject to discuss at length. I may mention, however, I have never found any value in the nature of the cells present as a means of localising the site of a lesion of the genito-urinary tract.

A detailed bacteriological examination is always worth while. I would especially recommend it in separating a clinical from an actual cure in cases of *B. coli* pyelitis. If the patient is clinically in good health, but *B. coli* are still present in the urine, it is probable that a recurrence will take place if treatment is not continued until the urine is germ free.

(7) *Value of blood analysis.*—We have now had sufficient cases examined by the staff of the biochemical laboratory to have formed an opinion of the value of blood analysis as a clinical aid. The object of it is the determination of the renal functional activity. We have used it as an index of the value

of preliminary preparation carried out and as a guide to operation. In local renal lesions it is of no special assistance. Its value is, however, great in cases of backward pressure, especially when due to prostatic enlargement.

The non-protein nitrogen and urea nitrogen records of our cases have conformed to the standard of others. The estimation of creatinine has in almost all cases been much higher than, for example, those recorded by Bentley Squier. We have several times had patients with a creatinine reading well above his danger line who recovered after operation.

At first sight it appeared to us that the best confirmatory diagnosis of congenital cystic kidney would be by blood analysis. This is not so. The congenital cystic kidney is like the diseased but compensated heart. Except in their terminal stages what they both possess is not a lack of functional efficiency but functional reserve efficiency. Thus, we have had cases where although the disease was pronounced the blood urea record was normal. In one such case, however, in which a carcinoma of the splenic flexure was suspected, after an exploratory operation the blood urea record rose to over 100 mg. urea nitrogen per 100 c.c. of blood and the patient gradually sank and died.

Each case investigated presents its own problems for solution. With time, patience and adequate appliances most can be solved. One class of case has proved specially difficult and it is advanced tuberculous disease of the kidney with tuberculous disease of the bladder, rendering bilateral ureteral catheterisation difficult. Usually in such a case one ureter can be catheterised. If in the sample of urine from that side tubercle bacilli are present and these germs are also found in the sample of bladder urine, the problem is—is the other kidney also affected by tuberculous disease?

The plan I have followed has been to repeat the examination under a general anæsthetic, and if this fails, to arrange for suitable constitutional treatment in convalescent home or elsewhere for a month before again examining the patient. When, as has happened to me twice recently, success attends this examination and unilateral renal disease is revealed, I have followed the course of removing by operation the diseased organ.

Discussion.

Sir David Wallace said he had been much interested in the important paper which Mr Wade had read, but the field it covered was so large that it was impossible to discuss the various points in detail. Mr Wade had referred to two Schools in connection with clinical work —the Materialistic and the Idealistic. Sir David fancied that the majority would like to belong to the idealistic, while taking advantage of the materialistic, but there was no doubt that there was a tendency at the present time to throw over clinical observation and trust too much to specialised methods. This, he thought, was a mistake. In his remarks, Mr Wade took no note of what, in the speaker's opinion, was important in connection with renal cases—that is the influence that the diseased kidney had upon the healthy kidney. He believed a stone in one kidney not infrequently produces pain in the other kidney and influences its function. While he did not believe that in the majority of cases there was any risk in ureteral catheterisation, he did believe that in some cases the catheter temporarily induces changes in the function of the kidney. Mr Wade alluded to hæmaturia, and stated that in a difficult case the passage of a catheter into the pelvis of the kidney induces bleeding and enables the affected kidney to be determined. He himself was very doubtful if this is reliable. No doubt if the affected part could be reached by the catheter, bleeding might be induced, but how frequently would this not be so. Regarding radiography to determine the position of a ureteral calculus, and to differentiate between a stone in the ureter and a calcareous gland external to it, a ureteral catheter which gave a shadow was of much value, but he would remind the Society that more than twenty years ago Harry Fenwick introduced a shadowgram bougie for this purpose, and in certain cases it was very valuable.

Mr Stuart described a case illustrating a possible fallacy in chromocystoscopy. The patient had a large tender left kidney and suffered from hæmaturia. Chromocystoscopic examination showed that no pigment was being excreted from the left ureter, while pigmented urine was issuing freely from the right ureter. The left kidney was removed, and at the last moment a second ureter was found emerging from near the lower pole. The man died, and post-mortem examination revealed the absence of a right kidney, and that the two ureters from the left kidney entered the bladder at the normal positions of the right and left ureters.

Professor Meakins said that he was glad that Mr Wade had taken such a conservative view about what the chemist could do to help the surgeon. By that he meant that, if the surgeon had a case about

which he was uncertain as to whether he was fit for operation, the chemist after certain examinations could help him, and more especially in cases where the patient looked fit but where on closer examination it was found that he was not fit. On the other hand, if it was found that the patient was not fit for operation and the treatment appropriate to the case was followed out, he thought that in time the chemist could give the surgeon an extremely accurate indication as to whether the treatment indicated an improvement or otherwise with regard to future operation. In regard to creatinine in the blood, it had been lately found that the serious prognostication of high creatinine in the blood might be quite wrong, as it was still to be definitely determined as to whether the present-day reactions to creatinine in the blood were exact. The more careful biological chemists were doubtful as to its accuracy and additional experimental evidence added to the suspicion. Further careful biochemical studies would determine the point at issue.

Mr Wade said, in reply to Sir David Wallace, that he had endeavoured to make it clear in his paper that it was only in those cases where a vascular tumour, such as a hypernephroma, had invaded the renal pelvis that the introduction of a ureteral catheter would be followed by the induction of hæmorrhage. In those cases where the tumour had not invaded the renal pelvis, naturally the introduction of a catheter would not be associated with the production of any hæmorrhage. It was in this latter class of case especially that most valuable assistance was to be obtained from the taking of a pyelogram which would reveal the characteristic appearances of tumour growth in the lengthening, and later destruction, of the calyces in the region of the kidney in which it was situated.

As regards the early diagnosis of renal tuberculosis Sir David Wallace had raised his hopes when he referred to the recognition of an early focus of tuberculous disease situated in the cortex without the pelvis being invaded. In recognising such cases, the difficulties of exact diagnosis were very great and much had still to be learnt. It would appear that in many of them exact diagnosis would only be obtained when the kidney had been exposed by operation.

Mr Stuart's case was one of great interest. As has been already mentioned a single functionating kidney was of frequent occurrence. A double ureter with two ureteral openings into the bladder was also frequently met with. Mr Stuart's case was unique, however, in that as revealed by chromocystoscopy the bladder possessed two ureteral openings normally situated and from these pigmented urine was seen to be vigorously voided, while the operation revealed that these two channels came from a single kidney. As far as Mr Wade was aware,

no similar state of affairs had ever previously been recorded.* Its diagnosis of course would be an easy matter by an X-ray catheter or other means. The problem was—when was its presence likely to be suspected, so that such a detailed examination would be indicated?

Professor Meakins had most properly emphasised the valuable knowledge the biochemist could provide to the clinician. Mr Wade remarked that in recognising when a patient was really ill, or when his general health was good, the clinical instinct of the medical man with experience was seldom at fault. He had had two cases of prostatic enlargement where the patients looked in good health and appeared as if they would stand operative treatment well. The report from the biochemist, however, in both of them gave a dangerously high level of blood urea. In both cases the critical condition that developed after operation supported the biochemist's grave prognosis.

* The most likely explanation of Mr Stuart's case would appear to be that it was one of a unilateral fused kidney.

In the *Journal of Urology*, volume vii (1922), page 321, Hyman records two such cases diagnosed during life by the use of X-ray catheters. In these cases the catheters entered ureteral orifices normally placed, but both passed to a fused kidney situated on one side.

Transactions of the Medico-Chirurgical Society of Edinburgh

SESSION CII.—1922-1923

AT a Meeting held on 1st November, the following were elected Office-bearers for the Session 1922-1923:—

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Transactions of the Medico-Chirurgical Society of Edinburgh

HYDROCEPHALUS.*

By JOHN FRASER and NORMAN M. DOTT, Edinburgh.

HYDROCEPHALUS has been regarded up to the present time as one of the most hopeless and unpromising of the diseases of childhood. The diverse methods of treatment which have hitherto been suggested have proved entirely unsatisfactory in the majority of cases. This unfortunate situation was dependent upon a lack of appreciation of the fundamental factors in the etiological pathology of the disease. Recent advances in this direction have made possible the application of scientific principles of treatment. It is of interest to note that Hilton, in 1844, had recognised a type of internal hydrocephalus in young children in which he believed that occlusion of the foramen of Magendie was the essential pathological element. He also describes a case in which the iter was obstructed and internal hydrocephalus resulted. Hilton's observations, remarkable as they were, provoked no practical advance in the treatment of the disease, and it is to the recent work of Dandy and his colleagues that we are chiefly indebted for the better promise which operative treatment now holds out. Since the publication of Dandy's original papers we have had the opportunity of investigating and treating a number of hydrocephalic infants and children, and we propose to submit the results of these experiences.

The Cerebro-Spinal Fluid System.—A consideration of the normal physiology of the parts involved is a necessary preliminary to the comprehension of etiological pathology and a necessity for rational treatment.

The Sources of the Cerebro-Spinal Fluid.—The choroid plexuses of the cerebral ventricles may be considered, for our

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present purpose, to be the sources of the fluid. This was clearly demonstrated by Dandy, who experimentally occluded the foramen of Munro, when extreme dilatation of the corresponding lateral ventricle ensued. When the choroid plexus was excised from a lateral ventricle so excluded, the cavity did not dilate, but collapsed. Conclusive proof was thus afforded of the source of the fluid in the choroid plexus. The fluid is probably produced by a process of active secretion, for it may attain a high pressure, and the cells which transmit it from the blood exercise a highly selective power. Instances of this capacity are seen in the absence from the fluid of bile pigment in jaundice, and the failure to recover many diffusible drugs from it when they have been administered.

Into the subarachnoid space the fluid of the perivascular spaces of the central nervous system finds its way. This probably corresponds to a drainage system analogous to the lymphatics of other parts of the body. While it contributes an addition to the cerebro-spinal fluid and represents, no doubt, an important function, the quantity so added is inconsiderable in relation to hydrocephalus, but it is of importance in the production of certain subarachnoid cysts to which we shall refer later.

The Absorption of the Cerebro-Spinal Fluid.—Absorption of cerebro-spinal fluid takes place from the subarachnoid space. For our present purpose we may consider the site of absorption to be the subarachnoid space overlying the cerebral hemispheres. The return to the blood stream of the fluid is the function of certain specialised structures derived from the arachnoid membranes—the arachnoid villi, the Pacchionian bodies and groups of mesothelial cells. Weed and his collaborators described and investigated the arachnoid villi. They are fine tortuous processes which arise from the outer surface of the arachnoid membrane, perforate the dura mater, and project into the cranial sinuses and larger cerebral veins near the sinuses. They are covered with specialised mesothelial cells from which the fluid is conveyed into the blood stream. The process is probably one of filtration and dialysis. The Pacchionian bodies are simply examples of aggregated and hypertrophied villi; their relations and function are exactly similar, they are met with only in man and certain anthropoids, and they are not developed in children. Nest-like groups of specialised mesothelial cells connected with processes of the

arachnoid are indiscriminately scattered in the substance of the dura, and by this means the fluid can reach the outer surface of the dura, where it is absorbed.

Another and less important path of absorption exists in the perineural lymphatic spaces of the cranial nerves; by this route cerebro-spinal fluid has been shown to reach the cervical lymphatics, but we would again emphasise that the main absorption area is that over the cerebral hemispheres.

The Circulation of the Cerebro-Spinal Fluid. — Having established the source and destination of the fluid, we are now in a position to follow out its circulation. Starting in the lateral ventricles, it flows through the foramina of Munro to reach the third ventricle. Here its volume is augmented by the choroid plexus of that cavity, and it passes through the aqueduct of Sylvius into the fourth ventricle. The choroid plexus of the fourth ventricle furnishes a further contribution, and the fluid passes out into the cisterna magna of the subarachnoid space through the minute foramina of Magendie and of Luschka, which perforate the lower part of the ventricular roof. (The central canal of the spinal cord is of no interest in this connection and constitutes merely a blind diverticulum.) From the cisterna magna the fluid permeates upwards and forwards round the sides of the medulla and over the cerebellar hemispheres. In order to reach the fore-brain it must pass through that narrow isthmus of the subarachnoid space which surrounds the mid-brain, and is bounded by the free edges of the tentorium cerebelli and the basisphenoid, the roomiest part of this passage being the cisterna interpeduncularis. From here the fluid is free to ascend over the cerebral hemispheres, where, as we have seen, its absorption occurs.

The fluid, after escaping from the ventricular system through the foramina of Magendie and of Luschka into the cisterna magna, may also pass caudally into the spinal theca. Very little absorption occurs in this area, but, while the spinal theca is of no significance as a circulatory pathway, it is of importance as being the most convenient anatomical site at which to obtain fluid from the subarachnoid area for investigation.

Before leaving the anatomy of the pathway of the cerebro-spinal fluid, we would draw particular attention to four points of constriction which lie in the route—(1) The foramen of Munro; (2) the aqueduct of Sylvius or iter; (3) the foramina of Magendie

and of Luschka; (4) the tentorial isthmus around the mid-brain.

It will be noted that the first three are situated in the ventricular system, the fourth in the subarachnoid space. These four constrictions are the points of pathological incidence in hydrocephalus.

The Essential Error in the Formation of a Hydrocephalus.—A hydrocephalus is an undue accumulation of cerebro-spinal fluid within the cranial cavity. Considering its possible etiology in the light of the foregoing description of its formation, circulation, and absorption, how may it arise? (*a*) It might be caused by an excessive production of fluid; (*b*) it might be caused by an obstruction in the route of its circulation; (*c*) it might be caused by a deficiency in its absorption.

There is little ground for believing that excessive production of fluid is a cause of hydrocephalus. It may occur in the "acute hydrocephalus" of infective meningitis and ependymitis, but this condition is hardly to be included here. It is, moreover, doubtful whether in it "an undue accumulation of cerebro-spinal fluid" exists, for the fluid obtained in such cases partakes more of the characters of an inflammatory exudate, and may not, therefore, have its origin in the choroid plexuses. Another possible mode of over-production of fluid has been suggested as a consequence of obstruction to the vein of Galen, which drains the choroid plexuses of the lateral and third ventricles. Such an occurrence must be rare, and its consequences on the production of fluid uncertain, and we feel that for practical purposes it may be neglected.

Obstruction to the cerebro-spinal fluid circulation is the essential cause of hydrocephalus. It is liable to occur at the four anatomical points of constriction of the pathway which have been mentioned. The causes of such obstructions will be discussed with the etiological pathology of the disease.

Diminished absorption of the fluid has not been shown to exist apart from obstruction to its circulation.

A rare congenital type of hydrocephalus, predominantly external, occurs in association with gross developmental defects of the brain, but it is of no surgical interest, its victims usually dying within a few hours of birth, and it is included in our classification merely for completeness sake.

Classification of Hydrocephalus.—The older classifications

of hydrocephalus were not based upon scientific knowledge of the disease, and are now inadequate. Dandy has elaborated a classification, which, for surgical purposes, we have ventured to simplify.

We have stated above that a hydrocephalus predominantly external exists as a rare anomaly in development—we doubt whether a pure external hydrocephalus can ever exist. Certain subarachnoid cysts, the result of localised adhesions shutting off a limited area of subarachnoid space, which probably becomes filled and distended by the perivascular drainage, have recently been described as a form of external hydrocephalus, but such cysts are well known to occur in the spinal meninges, and the condition cannot be properly regarded as a hydrocephalus. We believe that increased production and decreased absorption can be ruled out for practical purposes, and we take cognisance only of the congenital developmental type, and the various forms of circulatory obstruction. The latter are naturally divided into ventricular and extra-ventricular obstructions, and the ventricular lesions are again subdivided according to their exact anatomical site :—

	Group	Degree (Site of obstruction)
Hydrocephalus due to	Congenital anomalies	
	Ventricular (obstruction)	1. Between one lateral and third ventricle.
		2. Between both lateral ventricles and third ventricle.
		3. Between third and fourth ventricles.
		4. In the roof of the fourth ventricle.
	Extraventricular (obstruction)—In the subarachnoid space.	

The above, we submit, is a simple, expressive, and accurate classification from the anatomical and physiological points of view. It is also significant practically, for, as will appear later, each type has its distinctive and appropriate treatment.

Recognising that all surgical hydrocephalus is obstructive, we omit the term in actual use, and speak, for example, of "a ventricular hydrocephalus of the fourth degree," or of "an extraventricular hydrocephalus."

The Etiological Pathology of Hydrocephalus.—*Congenital Developmental Hydrocephalus.*—This is the type which causes the gross enlargement of the fœtal head which may obstruct

delivery. The examples we have examined have shown a thinning out of the roofs of the lateral ventricles (which may be ruptured) and an absence of the quadrigeminal plate, so that the iter is open dorsally. The skull is largely filled with fluid, and the small, deformed brain is compressed forwards and downwards. Beyond the fact that it represents a gross and early error in development we can say nothing as to its cause.

The Etiology of Ventricular Hydrocephalus.—Ventricular hydrocephalus premises an obstructive lesion of the ventricular system. The chief causes of such obstructions are tumours, intracranial basal hæmorrhages, infective meningitis, and syphilitic meningitis.

Tumours are liable to cause hydrocephalus when, in virtue of their situation, they occlude the cerebro-spinal pathway. This may occur either at the foramen of Munro or at the aqueduct of Sylvius. At the foramen of Munro a cyst of the choroid plexus may cause occlusion. Professor Edwin Bramwell has kindly supplied us with particulars of such a case (unpublished) which came under his notice. At the aqueduct of Sylvius it is the tumour of the cerebellar-pontine angle which causes its compression, and it is of interest to note that the features of secondary hydrocephalus are apt to overshadow those of the tumour. The hydrocephalus is essentially a secondary one, and treatment is directed against the primary tumour. Regarding the hydrocephalus merely as a symptom of the tumour formation, we shall not consider the type further in this paper.

The remaining large group of obstructive lesions consists either in atresia of the narrow passages or of adhesions which obliterate the foramina in the roof of the fourth ventricle.

Basal Birth Hæmorrhage, when it occurs into the posterior cranial fossa and fills the cisterna magna, may leave firm plastic adhesions which extend across the interval between the cerebellum and medulla, and occlude the foramina of the roof of the fourth ventricle. In this way the cerebro-spinal fluid is pent up within the ventricular system, and cannot reach the subarachnoid space. In such cases the history of a difficult birth, which may have occasioned the use of forceps, is usual, and there is reason to believe that the sagittal application of forceps is specially liable to be followed by a subtentorial hæmorrhage, as contrasted with their lateral application.

Infective Meningitic Conditions are probably more frequent during infancy and childhood than is generally recognised. We believe that many otherwise inexplicable cases of ventricular hydrocephalus are caused by an antecedent lepto-meningitis. While such a meningeal inflammation may cause symptoms so mild as to escape notice, it may give rise to adhesions sufficient to occlude the minute foramina in the roof of the fourth ventricle. Should such an inflammatory condition spread and become an ependymitis, atresia of the aqueduct may ensue, and in this way ventricular hydrocephalus of the third and fourth degrees arise. We have observed one case in which infection from a cat suffering from distemper was followed by meningitis and subsequently by hydrocephalus, and another in which an acute periostitis of the occipital bone had a similar sequel.

Congenital Syphilis affects most severely the basal subarachnoid cisterns, where it causes the formation of plastic adhesions. As in the foregoing variety, the foramina of the roof of the fourth ventricle are liable to obliteration and ventricular hydrocephalus of the fourth degree results. Again, syphilitic ependymitis may cause an atresia of the iter. We believe that a large proportion of iter obstructions are the consequence of congenital syphilis, and that early antisyphilitic treatment will effect a cure without surgical intervention. It is of importance to note that a considerable proportion of hydrocephalics are the victims of congenital syphilis.

The Etiology of Extraventricular Hydrocephalus.—Extraventricular hydrocephalus premises an obstruction to the pathway of the cerebro-spinal fluid at some point in the subarachnoid space. We have seen that there is a narrow isthmus in the subarachnoid space where it passes through the tentorium cerebelli. This situation is the danger point. Dandy showed that, by the experimental production of adhesions around the mid-brain, hydrocephalus could be induced in dogs. The experimental evidence is entirely borne out clinically. In cases of extraventricular hydrocephalus, which we have had the opportunity to examine, post-mortem adhesions at this point were always found, and they can be demonstrated radiologically during life, as we shall see later. The causes of adhesions in this situation are similar to those which induce ventricular hydrocephalus of the fourth degree, namely, simple or syphilitic basal meningitis, and possibly basal birth

hæmorrhage. It is obvious that, if the fluid is shut off from its chief area of absorption, the obstruction will cause an increased pressure in the whole fluid system behind it, and, the cranium being least resistant to pressure in infancy, the lateral ventricles show the most striking dilatation. The spinal meninges and the subarachnoid space, though equally pressed upon, are better supported, and are therefore less distended.

Hydrocephalus and Spina Bifida.—We have placed this type by itself as the etiology is as yet obscure. That hydrocephalus may be present at birth in a child with spina bifida we have been able to confirm both at post-mortem and by ventriculography during life. It is well known that hydrocephalus may develop in an infant who is the subject of spina bifida, especially if the spinal defect has been closed by operation. The hydrocephalus is of the extraventricular type, and it appears feasible that a primary obstruction to the fluid circulation in the subarachnoid space around the midbrain, or a developmental error in the absorptive mechanism might account both for the spina bifida and hydrocephalus; the subject is at present under investigation.

The Morbid Anatomy of Hydrocephalus.—Little need be said on this subject, as its features are well recognised. There is a progressive distention of the ventricular system; the lateral ventricles are always most markedly affected in all types of the disease, as the resistance of the vault of the skull is less than that of the skull base or vertebral canal in the young child. The third and fourth ventricles and the subarachnoid space may show lesser degrees of distention according as the lesion affects the iter, the roof of the fourth ventricle, or the isthmus of the subarachnoid space. The vault of the skull enlarges, the brain matter of the cerebrum becomes thinned out, its sulci tend to disappear, the white matter may be almost entirely destroyed by pressure, while the grey matter is more resistant. The basal ganglia, by virtue of their protected position, are not liable to injury until late in the disease, and thus life may persist even when an enormous distention of the skull has been attained.

Our experience has been that the ventricular type has been more common than the extraventricular in a proportion of about three to one, and of the ventricular type, the fourth degree of obstruction preponderated over the third degree in a pro-

portion of eight cases out of fifteen. Personally, we have seen no examples of the first and second degrees of the ventricular variety.

Clinical Features.—The disease affects the sexes approximately equally; it is essentially an affection of the first year of life, but occasional instances of its occurrence may be noted in older children and even in adults.

The Clinical History.—The statement may be volunteered that the head was enlarged at birth. We do not feel convinced that much reliance could be placed on this statement in any of the cases we have observed, but it is quite possible that an intrauterine meningitis may occasionally occur.

Preceding the cranial enlargement a notable distention of the scalp veins may be observed. The enlargement is at first slow, but, having attained a certain point, makes rapid progress. No doubt a certain amount of intracranial accommodation can at first be made, but when this is no longer possible, and the resistance of the skull has been weakened by widening of the sutures, a rapid distention ensues. The axis of the eyes becomes displaced downwards and strabismus may be present. Optic atrophy occurs late in children, in contrast with its much earlier onset in adults whose cranial contents are being augmented. The mentality is wonderfully preserved, but, as distention increases, it becomes progressively impaired. General motor phenomena are of late onset, evidences of an irritative condition are twitchings and general convulsions, while the paretic phenomena are of the upper neurone type—paresis, spasticity, and increased deep reflexes: these motor disturbances may be asymmetrical. Babies suffering from hydrocephalus are usually emaciated and pale, of a senile aspect, and they may be very irritable. They usually feed well, but do not gain weight. The enlarged head cannot be supported by the neck, and it rolls backwards or forwards when the child is raised.

The Diagnosis and Localisation of the Lesion.—The presence of hydrocephalus is usually very obvious, but in order to locate and efficiently treat the causal lesion the following questions demand answer—(1) Is there any evidence as to the original cause? (2) Is the lesion ventricular or extraventricular? (3) If ventricular, what is the exact anatomical site of the lesion?

(1) *What was the Original Cause?*—As has already been

indicated, the possibility of syphilis as a cause is of the first importance, because antisyphilitic treatment may of itself be sufficient. A careful search must next be made for any indications of a localised intracranial tumour (this applies especially to older children). Having excluded these possibilities, which might entirely alter the line of treatment, there remain the birth hæmorrhages and antecedent meningitis and encephalitic conditions to consider. As far as possible their occurrence is elicited by appropriate questioning. Often no definite opinion can be arrived at, but, if we exclude syphilis and tumour, we are on safe ground, for in the other varieties the next step in the investigation is similar.

(2) *Is the Lesion Ventricular or Extraventricular?*—This is an important point to differentiate, for the treatment of the two types differs radically. The differential tests turn upon the fact that in ventricular hydrocephalus the fluid cannot reach the subarachnoid space, while in the extraventricular type it has free access to the spinal meninges, although it is excluded from those of the fore-brain. The tests are:—

(a) *Lumbar Punctures.*—As would be anticipated, the flow of fluid is slight and at low pressure in the ventricular type, while it is excessive and at high pressure in the extraventricular.

(b) *The Use of an Indicator.*—Following Dandy's recommendation, a neutral solution of phenol-sulphone-phthalein is employed for this purpose, and 1 c.c. of the solution is injected into one or other lateral ventricle through a needle which is passed *via* the anterior fontanelle. After an interval of five minutes lumbar puncture is performed, and the spinal fluid is withdrawn into a tube containing a few drops of 25-per cent. sodium hydrate solution. If the indicator has reached the spinal theca its pink colour is at once obvious (and it is quite distinct from accidental admixture of blood). It is obvious that its presence indicates an extraventricular lesion, its absence a ventricular obstruction. Dandy recommends an interval of thirty minutes, but in our experience five minutes is ample to decide the matter definitely.

If Ventricular, what is the Anatomical Site of the Lesion?—Should the obstruction be in the ventricular system, we must answer this question, and to do so the method of ventriculography is employed. It entails the replacement of the fluid contents of the ventricular system with a substance which can be radiologically recognised. Air has been largely employed for this

purpose, and we used it at first, but, while it satisfies the mechanical requirements, its employment is followed by a reaction of varying severity, manifested by pyrexia, irritability, and general ill-being of the child, which lasts from four to ten days. While the reaction has never occasioned us serious anxiety, it has constituted a definite objection to the method (and we understand that others have been less fortunate than ourselves in its use), and on the recommendation of Jüngling of Tübingen we have recently injected oxygen instead of air. No unpleasant *sequelæ* follow its use, and the relief of intracranial tension, which the procedure involves, causes a definite improvement in the patient's condition. The superiority of oxygen is probably partly due to its more rapid absorption, but also to the absence of some definitely harmful constituent of air, possibly nitrogen. Oxygen and air are equally efficient in delineating the ventricles radiologically.

The Technique of Ventriculography.—The apparatus employed for replacing the ventricular fluid by oxygen is figured (Fig. 1). It consists of a graduated jar inverted over water, in which the oxygen is contained. A 10 c.c. record syringe is fitted with a four-way stopcock, so arranged that, while the syringe is always in continuity with its lumen, the other three ways can be independently opened. These three ways lead respectively, by rubber connections—(1) To the needle in the ventricle; (2) to a waste receptacle; (3) to the oxygen container. The tubing should be of narrow bore (2 mm.), and between the syringe and the oxygen container a wool filter is interposed to ensure the sterility of the gas. The whole apparatus, with the exception of the oxygen container, is "dry," sterilised in the autoclave (not exceeding 5 lbs. per sq. inch of pressure).

A general anæsthetic is necessary. One lateral ventricle is punctured by way of the anterior fontanelle with a suitable hollow needle, and 10 c.c. of fluid is withdrawn into the syringe, which is now put in connection with the exit tube and the fluid expelled. The cock is turned to open the oxygen-intake tube, and the syringe filled with oxygen. Connection is again made with the needle in the ventricle, and the gas injected. This cycle of events is repeated as often as is necessary, the fluid being replaced by oxygen in small instalments of 10 c.c., so that at no time is the intracranial tension appreciably disturbed. If the position of the head is adjusted so that the needle occupies the most dependent

situation of the ventricular system practically all the fluid can be replaced. In practice 60-80 c.c. are replaced.

Radiograms are now taken (1) in the right lateral position, the left lateral ventricle being outlined; (2) the left lateral position, the right lateral ventricle being outlined; (3) with an inverted position of the head the photograph is taken in the sagittal axis, the gas rising as far towards the base of the skull (fourth ventricle) as circumstances permit. Positions 1 and 2 demonstrate that the foramina of Munro are patent; position 3 demonstrates at what level the gas is arrested in its attempt to rise towards the fourth ventricle. It will thus indicate whether the iter is the site of the obstruction or whether the gas has succeeded in entering the fourth ventricle, to be arrested at its roof.

A similar method of oxygen replacement of the spinal fluid by lumbar puncture may be utilised to demonstrate the site of the subarachnoid adhesions in extraventricular cases. After the oxygen replacement of the thecal fluid the patient is X-rayed in the upright posture, when the gas rises through the foramen magnum, and is caught under the tentorium cerebelli, which is outlined with remarkable clearness. If the subarachnoid isthmus is obstructed, the gas is stopped there, if it is patent, the gas enters the middle cranial fossa, and is distributed over the cerebral hemispheres, where it occupies the cortical sulci. A characteristic honeycomb appearance is reproduced on the X-ray plate corresponding to the distribution of the sulci (Fig. 8).

We have not employed this method as a routine in extra-ventricular cases, for in the treatment of these cases the lesion has not been directly attacked, and a knowledge of its exact site was of no particular value to us. Anticipating the possibility of more direct treatment, we hope to employ this method of investigation more frequently in the future.

Summary of the Investigation. — Having successfully prosecuted the investigation outlined above we have ascertained the following facts—(1) Whether the hydrocephalus *per se* demands treatment or not; (2) Whether the obstruction to the circulation of the cerebro-spinal fluid exists in the ventricular system or in the subarachnoid space; (3) The exact situation of the obstructive lesion. With these facts before us we are in a position to discuss the appropriate treatment of the case.

Treatment.—It is useless and entirely undesirable to carry

out any surgical intervention upon a child whose brain is already hopelessly destroyed by extreme expansion. While no definite rule can be laid down at present, we believe that a cranial circumferential increase of three inches beyond the normal represents roughly the dividing line between the promising and the unpromising cases. It is therefore a matter of the utmost importance that surgical relief should be given at the earliest possible opportunity. The child must, of course, be a reasonable "surgical risk," but the way in which apparently feeble infants have withstood the necessary operation has impressed us.

Of earlier methods of treatment little need be said. The majority aimed at intermittent or permanent drainage of the fluid from various sites, either externally or internally, but none of these attempts met with lasting success. Treatment by any form of medication was obviously doomed to failure. Of the earlier methods, that suggested and practised by Stiles alone holds its ground to-day. We shall refer to it in discussing the treatment of extraventricular hydrocephalus.

The Essential Difference in the Treatment of the Ventricular and Extraventricular Types. — In ventricular hydrocephalus we have to do with a narrowly localised and reasonably accessible obstructive lesion, and to the condition the principle of *restitute ad integram* is eminently applicable. Experience has shown that lasting benefit can accrue only from removing the obstruction, and so opening up the normal pathway.

In extraventricular hydrocephalus we are faced with a lesion less definitely localised and less accessible, and for these reasons we have felt that it was not justifiable to attempt a direct attack on the lesion. The treatment we have employed, therefore, is indirect, and aims at diminishing the production of fluid.

The Operative Treatment of Ventricular Hydrocephalus.— With the exception of the very rare first and second degrees of obstruction, *i.e.*, at the foramen of Munro, the surgical approach is by the suboccipital route. We have not had the opportunity of treating a case of the first-mentioned variety, and investigators should refer to Dandy's observations on this subject. The suboccipital operation aims at freely opening up the cisterna magna, from which access may be had to the roof of the fourth ventricle, or, by traversing that cavity, to the iter, and obstructions in either of these situations can be dealt with.

Preliminaries.—In cases with a high intracerebral tension

repeated tapping of the ventricles at intervals of a few days is a wise prelude to the sudden relief by operation. In all cases this should be carried out immediately before operation, as it reduces hæmorrhage, obviates the risks attendant on a sudden hernia cerebri, and facilitates intracranial manipulations. Precautions against loss of heat are, of course, particularly important during a prolonged operation upon an infant. The child is placed in the prone position, with the head bent forwards upon a special rest. The anæsthetic (ether vapour) is administered by intrapharyngeal insufflation through the nasal tube.

Exposure of the Roof of the Fourth Ventricle.—A midline incision is carried from the external occipital protuberance to the level of the seventh cervical spine. (The "cross-bow" incision, used in cerebellar operations on the adult, is unnecessary here—it involves additional bleeding, and closure of the muscles afterwards is less complete than the simple vertical incision permits). The dissection is carried through the fibrous intermuscular septum of the middle line, and the superficial muscular masses are retracted to expose the spine of the axis vertebra, the deep musculature of the suboccipital region, and the middle line of the occipital bone. It is undesirable to detach the trapezius from the superior curved line, but all the deeper muscular attachments between it and the foramen magnum are now detached from the bone with the periosteum in one mass on either side, and retracted outwards. In this way the occipital bone is bared from the superior curved line to the foramen magnum vertically, and to a similar extent laterally. By carrying this dissection accurately in the median plane, bleeding is rendered minimal, and the muscles remain uninjured, which is a point of importance.

Over each cerebellar hemisphere the skull is perforated by means of the drill and burr, and the openings in the bone are enlarged with a rongueur forceps until one large crescentic opening with its margins just inside the retracted muscles is effected. The convexity of the crescent is upwards, and its concavity corresponds to the posterior margin of the foramen magnum. It is of importance that the posterior margin of the foramen magnum should be removed, but that the section should not be carried towards its lateral angles lest the large posterior condyloid veins be injured. It is unnecessary to expose the lateral sinuses above. Bleeding occurs from the vascular bone

on each side of the foramen magnum and from the suboccipital venous plexus in this region, but it is readily controlled by means of bone wax and gauze plugs. The dura covering the posterior surface of the cerebellum is thus completely exposed.

An estimate is now made of the degree of intracranial tension which still exists, and which might render opening of the dura hazardous, and, if necessary, it is further reduced by lateral ventricular puncture. The dural sinuses, viz., the occipital and the two marginal sinuses, are secured close to the margins of the bone defect by ligatures carried round them on curved needles. The dura is opened by transverse slits on each side, and the opening is completed across the middle line by section of the falx cerebelli with fine probe-pointed scissors. The divided membrane retracts considerably, but additional room can be obtained by extending short vertical incisions upwards at either end of the transverse one, so as to form a flap above. Thus the posterior surface of the cerebellum, covered with its pia-arachnoid membranes, is exposed freely.

Between the cerebellum and the basis cranii a special retractor is inserted. The instrument carries two laterally placed blades, which lift each lateral lobe, and a small electric lamp between the blades, which illuminates the deep recess below the cerebellum. The cisterna magna is entered as the retractor tears the delicate arachnoid membrane. The cerebellum is very gently raised towards the vertex, and the back of the medulla and roof of the fourth ventricle are brought into view. If the roof of the ventricle is the site of obstruction, the view will probably be considerably obscured by adhesions, and the roof is often so distended backwards that it may be met and ruptured before the operator is aware of its proximity. On the other hand, adhesions may be so dense that distention has not been possible. In any case the condition is unmistakable, and relief is afforded by excising a diamond-shaped segment of the membranous ventricular roof, and in this way an exit for the cerebro-spinal fluid from the ventricular system is re-opened.

The Relief of an Iter Obstruction.—When the obstruction exists in the iter, the above measures will have exposed the normal roof of the fourth ventricle, and the operation must be carried a stage further. To gain access to the iter the fourth ventricle is laid open in its lower half by a vertical incision through its roof. The lower end of the vermis cerebelli usually must be split upwards in the middle line to give sufficient

access, and is apparently a harmless procedure. A small nasal speculum is inserted, and a view obtained of the upper terminus of the ventricle. A fine rubber catheter is insinuated and pushed upwards into the iter. If the obstruction resists the passage of the soft rubber catheter it is necessary to replace it by a graduated metal probe, which is forced very gently past the obstruction. The danger of incautious use of this instrument is obvious. Having overcome the obstruction, the soft catheter is again passed up the iter until the third ventricle is reached, an event which is demonstrated by a rush of cerebro-spinal fluid. In our earlier cases, following Dandy's advice, the catheter was left *in situ* for several weeks, but recently this measure has been abandoned, for the pressure of the cerebro-spinal fluid is apparently sufficient to maintain the channel after the obstruction has been mechanically overcome. In this way an occluded iter is re-opened, and exit afforded to the fluid pent up within the lateral and third ventricles.

Closure of the Wound.—Every precaution has been adopted during the operation to preserve the various layers traversed from avoidable injury. It is of the utmost importance that the wound closure be sound, as a leak of cerebro-spinal fluid is apt to be persistent, and septic meningitis is to be apprehended in such circumstances. An attempt is made to suture the dura completely, and the relief of tension which follows the operation often makes this possible. The overlying musculo-periosteal flaps are united by two layers of suture, and the skin wound completely closed.

In the immediate post-operative period it is necessary that the intracranial tension should remain low, to allow of consolidation of the wound. It usually remains low of itself, but any tendency to rise must be checked at once by ventricular puncture.

The Treatment of Extraventricular Hydrocephalus. — As already stated, we feel that a direct attack upon the extra-ventricular lesion is not as yet justified, for the lesion may be ill-defined, it is very inaccessible, and moreover it is this type of the disease which may undergo spontaneous arrest—such a fortunate event can hardly take place in the ventricular variety. If the obstruction cannot be overcome, all we have been able to do is to attempt to diminish the production of fluid. With this object in view, Stiles advocated ligature of the common carotid arteries, and in 1898 and again in 1912 he reported one or two favourable results. The method is obviously applicable

only to the extraventricular type, and the lack of definition between intracerebral and extracerebral obstructions in the past may explain to some extent the adverse criticism which it has received.

Dandy, with the same object of decreasing the production of fluid, has suggested excision of the choroid plexus (plexectomy). To attain success, it would appear that a plexectomy of each lateral ventricle would be necessary. The method is still *sub judice*, and we have hesitated to undertake an operation of such magnitude in a type of disease which may undergo spontaneous arrest.

We have treated all our cases of extraventricular hydrocephalus in which surgery appeared permissible by ligature of the common carotid arteries. The results, which are given in detail later, are not entirely satisfactory, but we believe they are of sufficient promise to warrant a continued trial of the method. The vessels are tied at the seat of election in the usual way. Only future experience can demonstrate the relative proportions of spontaneous arrests in the progress of the disease and of cures following carotid ligature, and such an estimate will be the only practical criterion of the value of the procedure.

Methods not directed against the obstructive lesion are at best unsatisfactory, and must of necessity remain uncertain in their results. The examination of specimens from this type of case at once impresses one with the impossibility of dealing directly with the actual adhesions which constitute the obstruction. The adhesions are, however, fairly limited in extent in the majority of cases. The tentorium and adhesions constitute an impassable barrier between the posterior and middle cranial fossæ, and, as this barrier is the cause of the hydrocephalus, we have considered the possibility of cutting a new opening in the tentorium to one side of the adhesions with the object of re-establishing the physiology, if not the anatomy, of the normal fluid circulation. Such a procedure is diagrammatically illustrated, and experiment upon the cadaver has assured us that the method is feasible.

In cases in which the X-rays show that limited adhesions exist we hope to make trial of this method, which certainly has a more phsyiological aim than those hitherto advocated.

Results.—Tables I. and II. summarise the cases and the results obtained. The cases of hydrocephalus associated with tumours are not included in this summary.

TABLE I.—*Ventricular Type.*

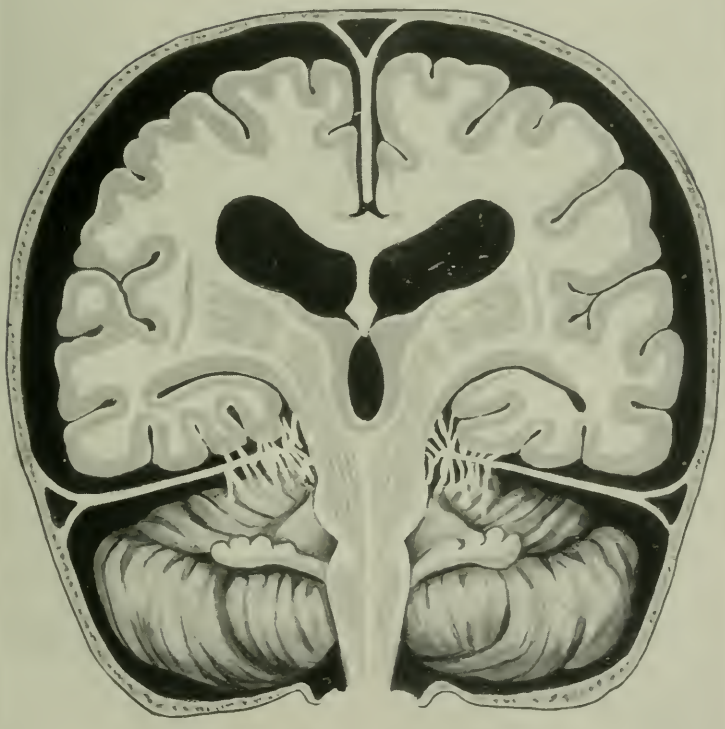
No.	Name and Age.	Degree.	Result.
1	J. S., 6½ months. . . .	4th	Died
2	E. A., 4½ months . . .	3rd	Died
3	E. H., 9 weeks	4th	No operation
4	A. Y., 10 months . . .	4th	Died
5	M. D., 5 months . . .	3rd	No operation
6	R. M., 3 months . . .	4th	Died
7	C. F., 7 months. . . .	4th	Cured
8	D. T., 7 months. . . .	4th	Improved (specific type)
9	N. S., 3 months. . . .	4th	No operation (died)
10	T. C., 1 year, 4 months . .	3rd	Died
11	M. M., 4 months . . .	4th	Cured
12	M. C., 3 years	3rd	Improved
13	J. H., 6 months	3rd	Cured
14	P. M., 8 months . . .	4th	Improved
15	L. C., 6 months. . . .	4th	Improved

At first sight the results appear to be unpromising—out of 15 cases the condition in 3 was so advanced as to preclude any prospect of success from operative interference, 5 cases succumbed from the operation, in 2 cases the operative interference has resulted in apparent arrest of the disease, but we do not classify these as cures because there has been no diminution in the bulk of the head, the mental condition has remained permanently impaired, and it is unlikely that these children will ever become useful members of society, capable of taking their share in the work of the world. In three instances (this is the hopeful side of the problem), it would appear that we have been successful in effecting a complete cure. In 2 cases insufficient time has elapsed since operation to justify classifying the cases, though, so far, the results appear to be very promising.

TABLE II.—*Extraventricular Type.*

No.	Name and Age.	Method Adopted.	Result.
1	R. W., 4 months . .	Ligature of carotids	Condition arrested
2	S. S., 8½ months . .	Do.	Do.
3	M. M., 1 year, 2 months	Do.	Condition progressed (fatal in six months)
4	E. S., 9 months . .	No operation	Succumbed on admission
5	N. M., 9 months . .	Ligature of carotids	Condition arrested
6	A. P., 10 months . .	Ligature of one carotid	Succumbed to hyperpyrexia within twenty-four hours of operation
7	J. G., 8 months . .	Ligature of carotids	Improved
8	J. M., 7½ months . .	Do.	Do.

1



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Out of a total of 8 cases of extra-ventricular hydrocephalus with carotid ligature 5 have very definitely benefited, and, though we do not wish at this stage to classify them as complete cures, we believe that everything points to a successful issue. The total series is, of course, too small to afford conclusive evidence, but the proportion of five improvements out of 8 cases has so encouraged us that we intend to continue to practise this method of carotid ligature in cases of extra-ventricular hydrocephalus in preference to the method of plexectomy.

DESCRIPTION OF PLATES.

FIG. 1.—The apparatus used in the intra-ventricular injection of O_2. The O_2 is contained in a water-sealed glass cylinder, and it is forced into the ventricle by means of a record syringe.

FIG. 2.—A semi-diagrammatic representation of the common situation of the lesion in extra-ventricular hydrocephalus—the adhesions are situated between the crura and the edge of the tentorium cerebelli.

FIG. 3.—Ventriculogram showing dilated right ventricle.

FIG. 4.—Ventriculogram showing an iter obstruction. The O_2 has occupied the right lateral ventrice owing to right side being uppermost.

FIG. 5.—Ventriculogram showing a high iter obstruction. The third ventricle is greatly distended.

FIG. 6.—Ventriculogram showing an iter obstruction and unequal distention of the lateral ventricles.

FIG. 7.—Ventriculogram showing an obstruction in the roof of the fourth ventricle.

FIG. 8.—Ventriculogram of a case of extra-ventricular hydrocephalus. The O_2 has passed out of the ventricles into the subarachnoid space.

DISCUSSION.

Dr Edwin Bramwell said that so far as he knew this was the first work on ventriculography in this country. Mr Fraser and Dr Dott were not only to be congratulated upon the conclusions they had arrived at by means of the method, but also upon the results which they had obtained by its application. The speaker was reminded of the case of a child, admitted to hospital when he was a house physician in 1897, in which Dr Alexander Bruce diagnosed a hydrocephalus as a sequel to basal meningitis. Sir Harold Stiles, who had operated upon the patient, succeeded in incising the membranes in the region of the foramen of Magendie with temporary improvement. Mr Fraser had said that he had never met with a case of hydrocephalus in a child, in which the condition had been determined by an obstruction at the foramen of Monro. This statement recalled to Dr Bramwell a case observed in 1900, when he was a house physician at the National Hospital, which was, he thought, perhaps unique in relation to the symptomatology of an acute hydrocephalus so produced. The patient,

a woman of 42, was admitted with a history of some ten days' illness. Previously she had enjoyed good health. Headache, giddiness, and gradually deepening coma had been the outstanding symptomatic features, a slight degree of papillitis was present. The coma deepened and the patient died the day after admission. At the post-mortem the lateral ventricles were found to be dilated; while in the third ventricle there was a simple cyst, growing from the choroid plexus and situated between the pillars of the fornix, which had plugged the foramen of Monro like a cork, and had thus caused death. The facts suggest that if the foramen of Monro is blocked death may result within a fortnight, as a result of the acute hydrocephalus so produced. This case was also of great interest in relation to the symptomatology of acute hydrocephalus, a consequence of an obstruction in this region. Although the case had been briefly reported, with an illustration, in Batten and Collier's classical paper upon the "Spinal Cord Changes in Cerebral Tumours," it had not hitherto received attention in the present connection. Dr Bramwell referred to another instance in which death was attributable to a cyst in the same situation. In this case the organs had been demonstrated to the Society by the late Sir Thomas Fraser as illustrating transposition of the viscera.

Dr Ker asked if Mr Fraser had satisfied himself that the cause of hydrocephalus was always obstructive? He himself had, in treating cases of cerebro-spinal meningitis, observed hydrocephalus in the making, and, while obstruction was doubtless a common cause, it appeared to him that, in some cases at least, irregularities of either the production or the absorption of the fluid were responsible. It was customary nowadays, during the convalescence of meningitis, to use lumbar puncture on very slight indications of a collection of fluid in the ventricles, and such punctures might have to be repeated over a long period. As they always relieved symptoms, it was improbable that there was any obstruction. On the other hand, in the 1907 epidemic, before lumbar puncture was used as freely as it was to-day, these cases, in his experience, went on to chronic hydrocephalus. Serum treatment had done much to prevent hydrocephalus, but occasionally, obviously obstructive cases occurred in patients who were not admitted early enough to benefit from it. In such cases, in the future, he would be encouraged to call upon Mr Fraser for surgical assistance.

Miss Herzfeld said she wished to emphasise the good results obtained by anti-syphilitic treatment in cases of hydrocephalus due to congenital syphilis. She had recently treated two such cases, both of which had improved greatly. In one case, the Wassermann test in father, mother, and child were all negative, but, struck by the appearance of the infant, she treated it with N.A.B. with complete

arrest of the condition. She later discovered that the father had previously been under treatment for syphilis.

She was interested in the after-history of these cases, and wondered how Mr Fraser's cases would do ultimately. She had recently seen a boy of 12, on whom Sir Harold Stiles had operated in infancy, when he ligated both common carotid arteries for hydrocephalus. This boy, she was sure, would become a criminal. He was mischievous, disobedient, and deceitful, and gave a lot of trouble at home. She had seen him several times at the Children's Hospital, and the sisters and nurses agreed that his behaviour was exceptionally bad.

Dr Traquair asked whether Mr Fraser could say what was the prognosis as to vision in the operated cases, and whether the development of optic atrophy, which sometimes occurred, was preventible. One of the children shown had an internal squint of the left eye. He presumed this was a paralytic squint due to interference with the left sixth nerve. Cushing had shown that in cases of high intracranial pressure the sixth nerve might become compressed between the pons and a branch of the basilar artery. Could Mr Fraser say whether this cause operated also in hydrocephalus, and whether the paralysis was relieved by the operation? Mr Fraser had said that external hydrocephalus was always associated with internal hydrocephalus. Was internal hydrocephalus always associated with external hydrocephalus? He supposed not. Could the pressure in the lateral and third ventricles rise to a much higher level than the pressure on the outside of the brain? He gathered that it could, but would like definite information on that point.

Mr D. M. Greig desired to emphasise the frequency with which hydrocephalus occurred in inherited syphilis. In many children the hydrocephalus became spontaneously arrested, but mental deficiency persisted. A considerable number of such children were to be found in the institutions for mentally deficient children throughout the country. For assistance in other lines of research he hoped Mr Fraser would append to everyone of his case-reports the results of the Wassermann reaction in the child, and also, if possible, in the mother or parents.

Dr J. S. Fraser.—Mr John Fraser's paper is of great interest to the otologist, who has to deal with cases of acute purulent meningitis resulting from suppurative otitis media. Purulent meningitis is by far the most dangerous complication of middle ear suppuration. While we obtain a cure in from 60 to 70 per cent. of cases of septic thrombosis of the sigmoid sinus, and in from 30 to 50 per cent. of brain abscess, we consider ourselves lucky if we have a good result in 10 per cent. of cases of meningitis. About ten years ago, in a case

of purulent meningitis, I performed an operation very similar to that just described by Mr John Fraser. (This operation was introduced to otologists by two of their American colleagues, Kopetzky and Haynes.) The result was not successful, and, as far as I know from reading the literature, there has been no case of cure of purulent meningitis from the drainage of the cisterna magna. I believe, indeed, that the operation has been abandoned, and that otologists now confine themselves to clearing out the focus of infection in the middle ear, and draining the lateral cistern by opening up the labyrinth, and through it the internal auditory meatus. At post-mortem examinations on cases of purulent otitic meningitis I have been struck by the marked collection of pus between the upper surface of the cerebellum and the lower surface of the tentorium, while the surface of the cerebral hemispheres themselves remain almost entirely free from purulent exudate. I had always looked on this area between the cerebellum and tentorium as a sort of "backwater" in which the pus collected, but Mr Fraser's explanation of the course taken by the cerebro-spinal fluid after leaving the fourth ventricle clearly explains these appearances. I should like to know from Mr Fraser whether he thinks that lumbar puncture, combined with puncture of the lateral ventricle, and injection of oxygen or fluid into the lateral ventricle, holds out any hope in the treatment of purulent otitic meningitis. I do not see why translabyrinthine drainage of the lateral cistern might not also be resorted to in conjunction with the above measures—the idea being to wash out the subarachnoid spaces of the brain and spinal cord by means of fluid introduced through the needle or trocar in the lateral ventricle..

PRIVATE BUSINESS.

Meeting—1st November 1922.

The following were elected Members of the Society:—William R. Martine, M.B., C.M., Haddington; Anderson G. M'Kendrick, Lt.-Col. I.M.S. (retired), M.B., M.R.C.P.E.; John J. Wilson, M.D., M.R.C.P.E., Anstruther; Leybourne S. P. Davidson, M.B., Ch.B., M.R.C.P.E.: John Jardine, M.D., D.P.H., F.R.C.S.E., Liberton; George E. Martin, M.B., Ch.B., F.R.C.S.E.; G. L. Malcolm-Smith, M.B., Ch.B., M.R.C.P.E.; Norman Dott, M.B., Ch.B. Edin., Colinton.

EXHIBITION OF PATIENTS.

Professor G. Lovell Gulland showed—(1) a case of **Addison's Disease.** Male, aged 42, suffered from pleurisy with effusion, 1894, a tubercular rib removed and left-sided psoas abscess opened 1902. Dysentery with malaria twice in India in 1896, dysentery in France again in 1915 while in the Army. In April 1922 had two attacks of hæmatemesis from which he recovered completely. Ten weeks ago was seized with sudden intense abdominal pain, with a rigour, which was followed by diarrhœa, with blood and mucus in the stools, which lasted for a fortnight, and was associated with temperature. The diarrhœa continued until his admission to hospital. During the early part of his stay in hospital our attention was concentrated principally on his intestinal symptoms. The various organisms causing dysentery were sought for, in vain, repeatedly, no tubercle bacilli were found in the stools. After he had been in the ward for about a fortnight it was noticed that his colour was becoming darker, and pigmentation was found inside his mouth, on the gums, and inside the cheeks, which increased rapidly from day to day. It appeared that early in the year he had been given arsenic by his doctor—no arsenic could now be found in the urine, nor in the hair or nails. The blood pressure varied considerably, but tended always to be rather low, successive readings at intervals of two days were, 118, 102, 135, and 115. Wassermann negative. Blood sugar 167 mgms. per cent.—a high reading—and his sugar tolerance was low. The blood shows a slight secondary anæmia. There is considerable myasthenia, but digestive symptoms have disappeared. The interesting point about the case is that what is presumably an "Addison's Disease" should have developed while he was in the hospital under observation for another condition. The heart is feeble, the lungs normal. He is to be treated with large doses of suprarenal and tuberculin.

(2) A case of **Polycythæmia Vera.**—A woman, aged 47, who had always been healthy until she had an operation for uterine prolapse eighteen months ago. This was followed by severe hæmorrhage lasting twenty-four hours, and the menses have not recurred since. Since her operation she has not felt well, easily tired, breathless, and depressed, with a feeling of fulness in the head and at first flushing. There has been no further bleeding. About a year ago she noticed that her colour was high and that she easily got cyanosed on exposure to cold or exertion. She was first admitted to hospital in February 1922, and remained until the beginning of April. The heart was normal, rather forcible, the spleen extended 2½ in. below the edge of the ribs and was hard. The red count at first was 11,280,000; hæmoglobin, 150; colour index, .7; whites, 26,800, with

fairly normal proportions. She was treated by the application of X-rays to the long bones, and during that period had two successive courses. Her count when dismissed was: reds, 9,500,000; hæmoglobin, 115; colour index, .65; whites, 18,600; the intervening counts varied, they were never again so high as on the first occasion, and the second last count was 8,500,000. She felt well until September when her symptoms came back, and on readmission it was found that the spleen was of the same size as when she was first seen, though it had become smaller during her first stay. The red count was 10,500,000; hæmoglobin, 145; colour index, .7; whites, 17,000. On this occasion she was only able to stay in hospital for about ten days, and had only four applications of the X-rays. The spleen became a little smaller, she improved generally, and her red count dropped to 10,000,000, the whites to 11,800. It will be necessary in this case to continue radiation at intervals for a very long period. All other possible sources of polycythæmia could be excluded.

Dr Cranston Low showed—(1) a case of **Lupus Carcinoma** on a man, aged 54. The lupus vulgaris had been present for eighteen years. Six months ago a raised, hard, warty lesion appeared on the lupus scar over the lower end of the left sterno-mastoid muscle. The lesion grew to the size of half-a-crown in six months. The patient had never been treated with X-rays. A cast was exhibited showing the condition before treatment, which consisted of scraping with a sharp spoon under a general anæsthetic. The scraping was done by Mr Hartley. On the following days radium was applied on four areas for two hours on each area so as to cover the base of the growth. The radium was exhibited, and stress laid on the form in which it was applied. The radium had been mixed with porcelain and fused on to a silver plate so as to form a flat plaque, which was much more suitable for the treatment of skin lesions than radium in tubes. The object of the treatment was to produce a radium reaction which would cause swelling, infiltration with leucocytes and blockages of all the lymphatics at the seat of the growth. It was pointed out that excision with the knife was hardly successful as the disease practically always recurred. After scraping and the application of caustics or radium, the risk of recurrence was very much less than after incision.

(2) A case of **Actinomycosis of the Face** in a woman, aged 47. The lesion appeared three months ago below the left eye and gradually enlarged till now the whole left cheek was swollen, red, and indurated. In two areas there were small projecting masses from which pus was oozing. The pus was examined, but no ray-fungus found. A carious premolar in the upper jaw of the same side had been removed a week ago. Infection had probably occurred through that tooth.

Patient was not in the habit of sucking straws, but had an allotment at which she worked. Since giving the patient potassium iodide, gr. x tic. a week ago, the lesion has become considerably less.

(3) A case of **Hebra's prurigo** in a youth, aged 15 years. The case showed the typical indurated dermatitis of the arms, thighs and legs, with enlarged hard glands in the axillæ and groins. He had had the condition as long as he could remember. He also suffered from attacks of asthma. It was pointed out that prurigo cases began in early life, with an eruption like urticaria papulosa, and persisted more or less all life, although tending to improve in adult life. It was always associated with eosinophilia in the blood, and was probably a sensitisation phenomenon. Such cases did not usually show any reaction to the food protein tests, but removal of infected tonsils had been reported as having a good effect. Many of the cases recorded of eczema alternating with asthma were probably cases of Hebra's prurigo.

CLINICAL MEETING.*

SIR ROBERT PHILIP, *President, in the Chair.*

EXHIBITION OF PATIENTS.

Mr Pirie Watson showed—(1) a case of **anterior dislocation of the hip-joint** produced by a motor accident, and which became a posterior dislocation during reduction. W. H., æt. 51, a stone-dresser, was admitted to hospital on the 7th October 1922, with a typical anterior dislocation of the left hip-joint and a few minor abrasions. He had been at work in a busy thoroughfare, seated on two granite paving-stones, dressing a similar stone which was placed between his extended and abducted legs. A seven-ton motor lorry, in passing, struck him on the left hip and knocked him over, but his left foot and leg seemed fixed. He felt a severe wrench at the left hip-joint, suffered excruciating pain, and was unable to rise or to move the left leg. On examination the left leg was everted, abducted, and flexed at hip and knee, the trochanter was sunken, and a prominence was visible in the groin which felt like the head of the femur. The femoral pulse was felt over this prominence. Anterior dislocation of the left hip-joint was therefore easily diagnosed, the head of the femur lying on the os pubis. Under chloroform, the manipulations first suggested by Bigelow were carried out, the patient lying on a low couch and an assistant fixing the pelvis by pressure over the iliac crests. The knee was fully flexed on the thigh, and the thigh flexed on the abdomen, the abducted and everted attitude of the limb being maintained. Circumduction inwards and extension was next performed, but instead of reduction the head of the femur slipped past the acetabulum into the position of posterior dislocation. The manipulations for posterior dislocation were immediately successful, the femoral head slipping easily into correct position. The after-treatment consisted of rest, gentle movement, and massage. At the end of three weeks he was allowed up, using crutches for a few days, but soon walked without aid and without a limp.

This case would not be worthy of recording were it not that it illustrates two points:—1. The mechanism of the production of anterior dislocation of the hip-joint. 2. The ease with which anterior may become posterior dislocation during the manipulations for reduction.

1. The force which produced the dislocation was comparatively moderate in nature. It is probably unique to have such an injury produced by a blow from a passing motor vehicle. In this instance

* Held 15th November 1922.

the momentum of a heavy lorry, moving even at a moderate speed, must have been considerable. The mechanism of production, however, remains unchanged—a fixed lower limb, suddenly and forcibly abducted at the hip-joint by a force which carries the body away from the limb.

2. The ease with which the anterior displacement of the femoral head became posterior was somewhat of a surprise to me, although, on enquiry, I find this is not an uncommon occurrence. Certainly no undue force was used, and the probable cause was excessive internal rotation and adduction in the circumduction movement.

(2) A case of **avulsion of the right anterior superior iliac spine** by powerful contraction of the sartorius. J. R., æt. 18, on the 23rd September 1922, attempted, with his right foot, to kick a football in the air, but missed it. He felt something snap in his right groin, fell, and was unable to move the limb without great pain. His doctor examined him on the field and felt crepitus at the anterior superior iliac spine, diagnosed avulsion of the spine, and sent him to the Royal Infirmary, Edinburgh.

On examination there was swelling, discoloration, and tenderness around the right anterior superior iliac spine, and pain on movement of the right hip-joint. X-ray examination confirmed the diagnosis of avulsion, and showed slight downward displacement of the spine.

The limb was put up in a double-inclined plane to relax the sartorius, and massage was commenced. At the end of two weeks flexion movements were allowed, and at the end of three weeks extension movements were commenced. Towards the end of the fourth week he was able to walk without pain, and a few days later was discharged to continue his convalescence at home. There was then palpable thickening around the iliac spine. This case seems worthy of record because the injury itself is rare, and because the mode of production is so simple and yet so typical.

Mr J. W. Dowden showed—two cases to illustrate the great **advantage of early active movement**:—(*a*) *Miner*, æt. 44, had, as the result of a blasting accident in 1918, a compound comminuted fracture of the lower third of the left radius and division of all the extensor tendons of the fingers, together with the radial extensors at the wrist. He had also a simple fracture of the upper third of the radius on the same side. The wound was cleansed, portions of bone and coal removed, and the tendons were then stitched with chromic catgut. A "cockup" splint was applied, and active movements of the fingers begun in twenty-four hours. The "cockup" splint was left off by day for periods, increasing in length, and only applied at night for a matter of six weeks. He is now at work as a miner with perfect function.

(*b*) *Female*, æt. 55, had a cut on the front of the left wrist with glass some five months ago. The cuts severed all the flexor tendons, the median nerve and part of the ulnar nerve. After careful cleansing, the tendons and nerve were united with catgut, and early active movement begun in the first twenty-four hours. The hand was kept in the flexed position mainly at night. All movements are practically perfect and the grasp is strong. Sensation is present in the nerve distribution, but she feels cold easily, and there is some tingling and numbness at the ends of the first and second fingers.

Miss G. Herzfeld showed—(1) two cases of **pseudo-coxalgia**. This is a condition variously known as Perthes', Legg's, Calvé's disease in Germany, America, and France respectively. It also goes under the name of "Quiet hip disease," or "Osteochondritis juvenilis deformans." The condition is characterised by a painless limp coming on gradually—the patient being usually a boy between the ages of 5 and 9. On examination of the affected hip-joint we find, briefly, limitation of rotation and abduction, but otherwise very few of the signs characteristic of tuberculous disease, from which it can, in a number of cases, be differentiated clinically. The X-ray appearance is very characteristic, and shows changes in the head, neck, and acetabulum. The head becomes flattened and appears to be broken up into fragments, the neck is broadened and shows typical areas of rarefaction close to the epiphyseal line, while the acetabulum gradually becomes shallower and may also show rarefaction around the upper border. Treatment is directed towards taking the weight off the affected limb for three to six months, either by means of plaster-of-Paris or a hip-splint; but treatment really does not influence the course of events, and all cases recover without ankylosis. There is, however, some restriction of abduction and the trochanter remains prominent. The condition is not very uncommon. In investigating 150 X-rays of supposed hip-joint disease, Miss Herzfeld was able to identify 15 cases of pseudo-coxalgia.

The two cases shown—both boys of 7 years—had been under treatment and observation for a year, and both showed the typical condition. In one boy the lesion was bilateral.

(2) Two cases illustrating the use of the **abdominal pedicle graft** in the treatment of webbed fingers and cicatricial contractines in young children.

Mr Walter Mercer showed—(1) Case of **graft of fascia lata and cartilage to skull**. A. M., æt. 33, was wounded on the 31st October 1914. He was admitted to my care on the 24th February 1920, with the complaint that he was continually suffering from fits. *Examination.*—There is a gap of about 3 in. by 1 in. on the left parietal bone. The wound is healed, but is depressed and

adherent all round and very tender especially in the lower part. On coughing there is a marked impulse, causing considerable pain in the wound. Within the last three months he has had five fits, during the last of which he remained unconscious for nearly an hour. He cannot speak, and gradually he loses consciousness. He has occasional attacks of giddiness, particularly when he bends his head low. He has a certain feeling of unsafety and fear of being hit on the affected part. He wears a metal shield for protection. Headaches are particularly troublesome and severe in nature, and are mostly frontal in situation.

An X-ray photograph shows a gap in the left parietal bone of 3 in. by 1 in. In view of the symptoms and the possibility of the scar being adherent to the brain an operation was decided on, with the view to removing the adherent scar tissue and filling up the gap in the skull. A removal of scar tissue would probably lessen the number of fits, the freeing up of the scar round the scalp would lessen the headaches, while the filling up of the gap would remove the feeling of unsafety and render the wearing of a skull shield unnecessary.

Operation, 26.2.20.—A semi-circular flap was turned down to include the old scar and with the base inferiorly. A circular incision was then made right round the gap in the bone and about $\frac{1}{4}$ in. from its edge and the periosteum turned inwards towards the gap so clearing the bone. A shelf was now made right round the gap by cutting away the outer table with a right-angled gouge. All fibrous scar tissue was dissected away from the neighbourhood of the wound, and especially from the surface of the brain which was entirely freed of the scarred dura. The scar tissue of the brain being completely cleared away a free edge of dura was secured around the gap and this freed from under the bone. This dural gap was filled with a flap of fascia lata from the thigh, a piece of this being grafted in with the fatty side next the brain. This was accurately sutured to the free dural edge by several interrupted and then continuous fine catgut. A 10-in. incision was then made parallel and over the left lower costal margin and the costal cartilages exposed. A piece of this was then lined out to fill the gap in the skull. This piece was then sliced, cutting off the anterior half and leaving the posterior half to preserve the continuity of the costal margin. The piece of cartilage curled up with a nice convexity which fitted the curve of the parietal bone. Four holes were drilled on the shelf of bone with an electric drill, and the costal graft was accurately apposed to fit the gap and stitched with catgut to the four holes. The scalp was then stitched down in place with interrupted silk-worm gut. The stitches were removed in twelve days, the wound being completely healed; there had been no discharge of cerebro-spinal fluid in the meanwhile.

26.3.20.—One month after operation he was discharged from hospital. He had no headaches, or fits since his operation. He was feeling and looking much better and was more cheerful. He has remained in communication with me since. The fits have practically disappeared, the headaches now cause him little trouble. On the 26.9.22 he writes: "Regarding my health, I am glad to be able to state that the last operation has done me a world of good. I seldom have a seizure now, and if I happen to have one it is only slight—never losing consciousness. I have headaches still, but not so severe as they used to be. I have more confidence in myself now, and can go to places without dreading having a seizure. I have one of the small holdings under the Board of Agriculture, and I also work in the Board of Agriculture."

(2) Case of **intra-medullary bone graft** for recent fracture of femur. K. B., a medical student, æt. 23, as a result of a motor cycling accident, was admitted to my care on the 23rd May 1921, suffering from the effects of the accident. On examination there was found to be—(1) A compound fracture of the left tibia, the fragments of which were in fairly good position; (2) a superficial incised wound down the right side of the nose and cheek; and (3) a simple fracture of the lower third of the right femur with the usual signs, but no crepitus could be made out. There was over 3 in. of shortening. X-ray examination showed fracture of both bones at the left ankle-joint; and a transverse fracture at the junction of the lower and middle third of the right femur with about 3 in. overriding of fragments.

Treatment.—On admission the wounds of the leg were swabbed with iodine and dressed and both legs put in splints, the left in a box splint, and the right on a double-inclined plane; 750 units of antitetanic serum were injected. 24.5.21.—Under a general anæsthetic the leg was pulled out as far as possible, counter-extension being maintained by a roller towel round the perineum, Pearson's ice-tong caliper applied, and the patient put back to bed. X-ray examination showed that the reduction had been incomplete, and there was still 2 in. of shortening. 5.6.21.—A further attempt was made, under chloroform, to correct the displacement of the lower fragments, and the leg was put in an inclined plane. This attempt was also unsuccessful, as shown by X-ray. Forty-five lbs. weight extension was now put on the Pearson caliper with a roller towel round the perineum to the head of the bed. X-ray still showed the fracture to be in an unsatisfactory position, and the shortening not reduced. It was accordingly decided to operate on the fracture. 11.16.21.—An incision was made along the lateral aspect of the leg, exposing the site of fracture. There was a considerable amount of blood clot and bruising of muscle at this level. By means of traction on the leg, and

manipulations with a heavy file between the ends, it was seen to be possible to get the fragments into good position. Retention, however, appeared to be the difficulty. It was decided to do an intra-medullary peg bone-graft. An incision was therefore made over the tibia on the same side, and a piece of the anterior surface of the tibia, about 6 in. long by $\frac{3}{4}$ in. broad, was removed by Albee's electric saw. The graft was now slightly sharpened at both ends and the electric reamer used for slightly widening the medulla of both femoral fragments. The graft was then inserted into the two fragments, and their position was found to be easily retained by this means. The wounds were then closed with catgut and silk-worm gut without drainage, and the leg was applied to a Miles' double-inclined plane.

There was an uninterrupted recovery from the operation, and the stitches were taken out on the thirteenth day; his knee movements started at the end of the first week. The inclined plane was left off on the twenty-first day, he was up on the twenty-eighth day, and out on the thirty-second day. No shortening resulted. X-rays showed good alignment and good union. The knee and ankle-joints gradually improved, although the extension of the knee was somewhat difficult at first. The patient is now able to do practically anything that he could do before the operation.

Mr George Chiene showed—Case of **goitre.** Female patient, æt. 56, operated on five years ago for large parenchymatous goitre. One lobe only removed. Now the other lobe is greatly enlarged and giving rise to pressure symptoms.

Mr J. J. M. Shaw showed—(1) a case of severe **trismus**, following upon fracture and depression of the zygoma and ankylosis of the temporo-mandibular joint. Treated by removal of the depressed portion or zygoma impinging upon the coronoid process of mandible and excision of the joint.

History.—Wounded, 28.6.18, with fracture of zygoma, malar bone, and condyle of mandible. Skin wound excised and sutured, leaving 2-inch linear scar below zygoma. Treated for six months by forcible opening of mouth by means of a "Jack" screw gag acting upon upper and lower dental splints. This painful treatment was abandoned in December 1918, when patient was discharged with an incisor gape of $\frac{1}{4}$ in. *On admission* to hospital, 2.10.22.—Bony ankylosis found to have supervened, with gape of $\frac{1}{6}$ in. Nutrition good, considering slit-like opening and loss of proper chewing movements. *Operation*, 20.10.22.—Excision of linear scar and subjacent scar tissue. Curved incision above zygoma behind hair line for exposure of temporal muscle and bone lesion at its insertion. Depressed anterior two-thirds of zygoma removed and major portion of condyle excised. A remnant of the cartilaginous meniscus, found at inner end of joint in healthy

condition, was left *in situ*, and a portion of the external pterygoid muscle drawn over the stump of the condyle to maintain mobility. No forcible stretching has been employed in the after-treatment, and the functional result, with gape of 1 in., is satisfactory.

(2) A case illustrating the use of the **tube pedicle graft** in chronic ulceration of the leg. *History.*—Wounded, 12.4.17, compound fracture of right tibia and fibula, lower third: injuries of left ankle necessitating amputation through lower third. Ulceration over site of fracture of tibia has persisted for five years in spite of two years' in-patient treatment, when five attempts at skin grafting were made, and two years' attendance at a hospital out-patient department. The ulcer was thinly healed over on one occasion for the period of a fortnight, but gave way on the first attempt at locomotion. *Operation*, 19.9.22—6-in. pedicle cut and tubed from excess skin on inner aspect of stump. The pressure points in relation to the artificial leg were avoided, and the free skin edges sutured without tension below the pedicle. 22.19.22, proximal end of pedicle divided, opened out, and sutured to healthy tissue at upper end of injured area. Limbs held in convenient nursing position by plaster spica above knees. The final stage for which patient is now ready will consist of (*a*) freeing of pedicle from left leg; (*b*) excision of scar tissue around ulcer; (*c*) opening of tube and suture in prepared bed.

Dr Douglas Guthrie showed—Case of **sarcoma of the tonsil.** Miss J. B., a typist, æt. 22, had suffered for four months from sensation of swelling in the throat, difficulty of swallowing, and "thickness" of speech. A swelling, the size of a pigeon's egg, of firm consistence and bright crimson in colour, occupied the right tonsillar region (water-colour drawing exhibited). The appearance closely resembled that of a peritonsillar abscess, for which many of the recorded cases of this rare condition have, in the first instance, been mistaken. The absence of pain and long duration of symptoms are significant facts in diagnosis. In this early case there were no enlarged cervical glands. The tumour was easily and almost bloodlessly dissected out under general anæsthesia, and was found to be limited by the capsule of the tonsil (specimen shown). Dr Dawson reported that the microscopic characters were those of endothelial sarcoma (cf. *Journ. Path.*, November 1918).

Sir David Wallace showed a case of **sarcoma of humerus.** B. N., a boy of thirteen years, in February 1922, complained of pain in the left shoulder after throwing a cricket ball. Three weeks later movement at the shoulder-joint was restricted, and a swelling was observed at the upper end of the humerus. On admission to the Infirmary, on the 4th April, the swelling was tender to the touch, firm, and elastic. There was no fluctuation present, and the diagnosis of

periosteal sarcoma was made. An X-ray photograph showed marked rarefaction of the bone, and in effect corroborated the diagnosis. Disarticulation at the shoulder-joint was performed—skin flaps being used. The operation was performed on the 16th April, and injections of Coley's fluid were begun. The patient made a good recovery, and went home on 22nd May. The patient returned to hospital in the third week of October, when it was found that recurrence in the axilla was present—a mass as large as an orange being palpable. The question of a second operation has to be considered, as there is no evidence of metastasis in the other organs.

Mr W. J. Struthers showed—Man, æt. 26, who had made an unusually complete recovery from a **contusion of the spinal cord in the cervical region**. At the time of the injury, two and a half years before he was shown to the Society, the patient fell 20 ft. into a hold, and as he fell he was struck by a hutch which fell with him. The exact mechanism of the injury could not be determined. Immediately after it the man was found to be suffering from paralysis of the upper limbs and trunk with very slight power of movement in the lower limbs; sensation was completely lost up to the level of the skin supplied by the fourth cervical segment of the cord; control of the bladder and rectum was lost. Recovery began within a fortnight of the accident and progressed steadily until, when shown, the patient was able to walk perfectly and to perform all movements with the hands and arms, except that he had difficulty in executing fine movements with his fingers, when he could not see what he was doing, *i.e.*, in fastening his collar-stud without a looking-glass. This incapacity was due to the fact that tactile sensibility had not fully returned in the hands. X-ray examination did not disclose any sign of injury to the spinal column, and the movements of the head and neck were perfectly free. The case illustrated an unexpected degree of recovery from an injury which, in its early stages, had all the appearance of becoming rapidly fatal.

Mr Henry Wade showed—two cases illustrating the results of **treatment of tumours of the bladder.**—(1) *Fulguration of Innocent Tumour* (*villous papilloma*). J. D., a male, æt. 42, suffered from persistent and painless hæmaturia which, on cystoscopic examination, was found to be due to two sessile villous papillomata. These were treated by fulguration in September 1920. The method of treatment by fulguration was originally introduced by Dr Beer of New York about thirteen years ago, and has since become the generally recognised method of dealing with such growths when circumstances permit. In this patient's case it was carried out, as is customary, without a general anæsthetic, and without the patient being detained in hospital. The treatment consists of destroying the tumour growth by means

of a high frequency current, the D'Arsonval bipolar current being employed, one electrode being introduced through an operating cystoscope and brought in contact with the base of the tumour growth, the other being a broad sheet of metal in contact with the patient's loins. The treatment was carried out on three occasions, at about a week's interval, so that at the fourth examination the tumour was found to have entirely disappeared. It was noteworthy in this case that, during his entire treatment, the patient did not require to spend a night in hospital nor did he lose a day's work. On re-examination, two years later, although the patient had suffered no discomfort nor had any hæmorrhage, a small tumour, similar in structure, was observed to have appeared close to the former site. This was dealt with in a similar manner to that employed on the previous occasions and is now removed.

(2) *Carcinoma of the Bladder*, involving right ureter, treated by excision and transplantation of ureter. G. G., male, æt. 59, suffered from persistent hæmaturia due to a large sessile tumour of bladder surrounding and involving the right ureter. He was treated by partial cystectomy and removal of the lower end of the right ureter which was implanted into the fundus of the bladder. The pathological report on the tissue removed was that it was a carcinoma, involving the bladder and ureter secondary to primary villous papilloma. Four months after the operation the healed site of the former operation was observed at the cystoscopy examination, and a minute, innocent, small villous papilloma was seen adjacent to the healed scar. This was treated by fulguration, so far without recurrence. Examination by chromocystoscopy and ureteral catheterisation showed the right kidney to be functionating, but to have a diminished functional activity as compared with the other kidney, a persistence of the condition observed prior to operation.

Dr Charles M'Neil showed—(1) Case of **sporadic cretinism**. M. M., æt. 9 years. Height, 2 ft. 9½ in., weight, 34 lb. Began to walk and talk between 3 and 4 years; and can now only say a very few words. Characteristic dull and quiet disposition on admission. Anterior fontanelle still open; delayed appearance of permanent teeth, and of ossification of other bones. After one month of thyroid treatment, has grown 1¼ in., and shows marked mental improvement.

(2) Case of **juvenile dementia and chronic syphilitic meringo-encephalitis**. W. E., æt. 13 years. For four years mental change noted by mother in the way of increasing timidity and childishness; also for two years increasing stiffness in walking, causing frequent falls. He shows, on examination, a general spastic diplegia, most marked in the legs, with great increase in all tendon

reflexes; also fixation of pupils with eccentric shape; fluttering tremor on closure of eyelids and protrusion of tongue. Speech is hesitating, and there is a habit of repeating single words. The behaviour is unnaturally bold and lacking in shyness, without any other definite mental change. Apart from disseminated chororditis and a doubtful atrophy of the upper central incisor, he shows none of the usual stigmata of congenital syphilis. The Wassermann blood reaction is positive, but cerebro-spinal fluid could not be obtained. The father died of aortic regurgitation five years ago, and in a family of four living children there has been one fœtal death. No evidence can be obtained of the patient having suffered from congenital syphilis in infancy and childhood.

Dr Robert A. Fleming showed—(1) case of **acromegaly**. A. C., female, æt. 27. Date of probable origin March 1922. There is typical enlargement of hands and feet and to less extent of lower jaw and tongue. The orbital arch is large, the zygoma, malar bones, and nasal processes also show increase in size. There is no enlargement of heart, liver, or spleen. A very early degree of bitemporal hemianopsia is present in the upper outer quadrants of the vision fields. Her chief complaints are headache, irritability of temper, and occasional pains in the legs. There is no glycosuria. X-ray examination shows deepening of the sella turcica and what appears to be a definite neoplasm of the pituitary. There is no optic neuritis at present, and Sir Harold Stiles, who has seen the case, agrees that operative treatment should be deferred.

(2) Case of **angina pectoris** with low blood-pressure. C. G., male, æt. 54, a labourer. *First attack* of typical angina occurred in 1910, when patient was carrying a heavy load of coals up a steep stair. *Second attack* occurred in 1912, under the strain of carrying a heavy load of bricks up a ladder. Each attack lasted for about two minutes, and the pain was described as shooting downwards and inwards from near the apex of the heart. Four attacks occurred between 1912 and 1922. In January 1922, he became very breathless, and suffered much from bronchitis. Since January he has had several attacks, varying in severity, and has been unable to work. His heart is dilated as a whole. Arteries show no marked arteriosclerosis. Pulse is slow—64 per minute—and regular. Maximum blood-pressure on admission was 98 mm. Hg. Wassermann reaction is negative. Electrocardiograms give no help. Great benefit resulted from the exhibition of digaline, arsenic, and strychnine. Explanation of anginous attacks may be localised spasm of heart wall due to a limited lesion of coronary circulation.

Dr John Eason showed—(1) Boy, æt. 17, complaining of intermittent pain in abdomen for past five years, shows (1) many signs

that may be attributed to sympathetic hypertonus; and (2) tenderness of the abdominal aorta. The patient's complaint is "abdominal pain," coldness, blueness, and chilblains of the hands. His doctor feared there was abdominal tuberculosis because of the pain, and because he felt "rather indefinite lumps in the abdomen." The latter, I believe, must have been due to constipation. Eighteen months later (November 1920), he wrote to say he could find no evidence of abdominal tuberculosis. In October of this year the patient was again suffering from pain situated higher in the epigastrium, and his doctor imagined he felt an enlargement of the left lobe of the liver. The condition actually appears to be an example of **dynamic dilatation of the abdominal aorta**—a disorder not unknown in the time of Hippocrates, and later accurately described by Morgagni as a cause of abdominal pain. This cause of abdominal pain is still occasionally overlooked to-day, and hence it is believed unnecessary operations have sometimes been performed. The pain and tenderness are, for the most part, solely along the course of the abdominal aorta and its bifurcations, but when intense, localisation is not so precise. There are both clinical and experimental facts in support of the hypothesis that dynamic dilatation is sympathetic, not parasympathetic, in origin, and its occurrence in this case showing evidence of sympathetic hypertonus is also suggestive. The same remark also applies to the vascular stasis and cyanosis seen in this case. The question has been put, "Would adrenalin be of any use in this case?" If my interpretation of the nature of the disorder is correct, I would expect to find adrenalin making the condition worse and pilocarpin improving it.

The highly complex phenomena of disturbed balance in the autonomic nervous system are difficult to analyse. In the Medical Out-Patient Department pharmacological tests cannot be used. Some knowledge adequate for diagnosis of the relative tone of the sympathetic and parasympathetic may be derived from the examination of the (1) oculo-cardiac reflex; (2) the state of the pupil; (3) the pulse of frequency; (4) the blood-pressure; (5) the differential count of leucocytes; (6) the behaviour of the gastro-intestinal tract as revealed by screening and radiograms. In young subjects without organic disease these tests are fairly adequate. With a minimum of inconvenience answers are obtained from different sectors of the entire autonomic system. By these tokens the patient shown presents harmonious evidence of sympathetic hypertonus. Thus (1) the oculo-cardiac test showed practically no slowing of the pulse, no respiratory arrhythmia, and no subjective discomfort; (2) the state of the pupil has always been widely dilated; (3) the pulse remains about 100; (4) the systolic blood-pressure is 138-40 mm. Hg. instead of 111

according to the formula for age (17); (5) the differential white count shows that 23.6 per cent. are large mononuclears; (6) screening and radiogram show gastric and intestinal stasis with deficient gastric peristalsis and pyloric spasm.

(2.) Three brothers, æt. respectively 17, 18, and 19 years, suffering from **nephritis.** Parents apparently healthy, one uncle died of nephritis; another uncle, according to report, suffers from chronic nephritis. One sister has always been delicate, and another, æt. 10, has presented symptoms which suggest that the integrity of the kidneys is doubtful. She had albuminuria for the first two days after admission to hospital for observation. The brothers present none of the stigmata of syphilis. The Wassermann test of the blood was in each negative. They are not known to have suffered from scarlet fever. The further investigation of these cases is proceeding with the object of determining the relative etiological significance of acquired and hereditary factors.

Dr Murray Lyon showed—Boy, æt. 9, a subject of **diabetes mellitus.** He had an attack of influenza in December 1920, but was otherwise healthy until May 1921, when thirst, polyuria, and increased appetite appeared. On 2nd June he was admitted to a hospital with a glycosuria of 10 per cent. (84 grm. in twenty-four hours). He responded at first fairly rapidly to treatment, but sugar frequently returned as the diet was increased. On 2nd November 1921, he was admitted to the Royal Infirmary, the glycosuria being then 3 per cent. (31 grm. in twenty-four hours). Fasting for one day made him sugar-free, and during three months he remained so, except for a very occasional trace. His diet was built up to 2,500 calories, including 70 grm. carbohydrate (21st February). No sugar appeared in the urine during the next three months. On 17th May a faint greenish tinge was got with Fehling. During the next few days the reduction became more definite in spite of fasting, and on 26th May an acute exacerbation of an otitis media was diagnosed. Glycosuria cleared up as soon as the discharge from the ear ceased. The patient again remained free from symptoms for a time. On 27th July sugar returned for a few hours following a slight accident, which excited him greatly. Recently he has had to return to hospital, because small quantities of sugar have frequently reappeared, in spite of careful attention to his diet.

Dr Frederick Gardiner showed—(1) Case of **tuberculosis of skin.** E. D., female, æt. 24. Operated on for glands in the neck at age of 10. Developed ganglion on the dorsum of the left foot at the age of 12. This swelling was operated on in Aberdeen Infirmary twelve years ago, but the wound never quite healed, and subsequently abscesses appeared on both arms, groins, and left calf.

This lasted for seven years, when they healed. Four and a half years ago the skin of the left leg began to be affected, and spread rapidly to the knee and then on to the thigh. The leg below the knee is œdematous and swollen, and there are thickened active areas on the left foot and also on the thigh. The whole condition points to spread along the lymphatics following the operation, and it is of interest as indicating tubercular origin of ganglion. She is being treated in the ward by inunction of 50 per cent. old tuberculin in vaseline once weekly and X-ray and trichloracetic acid lotion, and there has been a manifest improvement during the six weeks of treatment.

(2) D. B., æt. 21, male, grocer, developed **pemphigus foliaceus** six and a half years ago. The disease started on the shoulders in the form of small blisters and rapidly spread all over the body. At present all the skin area is involved; there is much exfoliation but very few vesicles. Since commencing treatment by the use of Condy baths and an ointment of bismuth oxychloride, he has slowly but steadily improved. The odour always associated with this condition has abated, and the general redness and tumefaction of the skin have subsided. The vesicles now only appear very occasionally on the hands and face. There is occasionally a slight temperature, and at present an eosinophilia of 7 per cent., but there are no other symptoms. Further, there is no previous history of a burn or injury as a precedent cause. The improvement, a very rare result in this disease, is in great part attributable to the youth of the patient and his persistent optimism. Recently he has improved still further following administration of injections of normal horse serum. A blood culture has been taken repeatedly, and a streptococcus has now been found.

Professor Meakins showed—a case of **enterogenous cyanosis**. F. R., female, æt. 42. At the age of 22 patient had gastric symptoms, associated with hæmorrhage, which pointed to the occurrence of gastric ulcer. This persisted on and off for some fifteen years, since which time there has been no more hæmatemesis. In March 1921, patient suffered from an acute attack of diarrhœa, which lasted for five weeks when it stopped suddenly, and constipation has persisted since. Towards the end of the period of diarrhœa or at the beginning of the period of constipation, cyanosis gradually developed, which became progressively worse with periods of relative remission. On physical examination the heart and lungs are normal. Abdomen is not distended, but rather a "doughy" consistency; some slight tenderness in the epigastrium. An opaque meal shows active gastric peristalsis with slight delay at the end of six hours. No deformity of the stomach. There is definite stasis of the meal through the small intestine, the stasis not being particularly evident at the ileocæcal

region. A good example of small intestine stasis is visualised as if some reflex cause were at work. Cæcum is slightly larger than normal, and there is definite cæcal stasis. Examination of the blood shows a normal red cell-count. Hæmoglobin estimation is difficult on account of a slight yellowish tinge to the blood. Spectroscopic examination shows, only in a strong solution of hæmoglobin, a band (in the red area of the spectrum) which occupies a position indicative of alkaline methæmoglobin. In addition to this there is a very pronounced shift of the oxyhæmoglobin curve to the right. The arterial blood is 88 per cent. saturated with oxygen. Carbon dioxide content normal. The cause of the cyanosis is due to the change of the oxyhæmoglobin curve plus a small contributing factor due to the presence of methæmoglobin. The causes of these changes in the hæmoglobin have not as yet been determined.

Dr W. T. Ritchie showed—a case of **malaria complicated by nephritis.** ——, clerk, æt. 22, had suffered from scarlet fever, without complications, at the age of 4. In Septemher 1921, while convalescing from amœbic dysentery, he contracted benign tertian malaria in Java. A week later he presented signs of acute nephritis. Subsequently he had recurrent attacks of benign tertian malaria, the last being on 8th September 1922. Now, he presents a secondary anæmia, the red cells numbering 3,720,000 per c.mm., the leucocytes 5500 per c.mm., and hæmoglobin equal to 60 per cent. There is persistent albuminuria with tube-casts, the urea concentration test is 0.9 per cent., and the non-protein nitrogen of the blood is 80 gmg. per cent. The Wassermann reaction is negative. The blood-pressure is normal. The case is of interest because nephritis is a rare complication of benign tertian malaria.

INFLUENZA, CEREBRO-SPINAL MENINGITIS, AND EPIDEMIC ENCEPHALITIS.

Some Etiological Considerations.*

By ALEXANDER JAMES, M.D., F.R.C.P.

Cerebro-spinal meningitis manifested itself in a marked epidemic form in Edinburgh in 1906, and rapidly increasing in severity and extent, it attained its maximum about the beginning of 1907. Diminishing rapidly during the remainder of 1907 it diminished more gradually during 1908 and 1909, and during 1910, 1911, 1912, and 1913 the disease at least, as regards frequency, was practically sporadic. In 1914 it burst out again, attaining a maximum about the end of that year and the beginning of 1915. It then declined much more slowly and gradually than in the earlier manifestation, till 1919, since then its severity has not been great.

Concerning these two manifestations, the first point which needs recognition is that the second and milder manifestation must be regarded as in a way accidental, and due to the gathering together in Edinburgh and neighbourhood of the large bodies of men required for the war. In evidence of this, I would point out that whilst in the 1907-1908 manifestation the proportion of children affected was immensely the greater, in the 1914-15 manifestation the reverse was the case. Thus, in the earlier manifestation, during the years 1907 and 1908, out of 140 cases, 40 were over 15 years of age and 100 were under it; whilst during the later manifestation, out of the 64 cases treated during the year 1914-15, 32, or one-half, were over 15 years of age, 30 of these being soldiers or sailors.

The general run of these two manifestations of the epidemic is shown by the lines (A) and (B) on the chart, the line (A) representing the number of deaths in Edinburgh from the disease, and the line (B) representing the number of cases notified in Edinburgh at the same time. As will be seen, the mortality line and the notification line clearly correspond, and as will be seen also so closely approximate, that the case mortality of this disease is made appallingly evident.

Indeed, it may be said that during the years 1911, 1912, and 1913 the mortality line and the notification line were practically

* Read 1st November 1922.

the same, a fact which demonstrates not only a very high case mortality, but the fact that C.S.M., in its earlier stages especially, may easily be mistaken for some other infectious disease—influenza, pneumonia, typhoid—and notified as such, be sent to hospital.

Let us now compare this C.S.M. curve with influenza (E).

Influenza has often showed itself in epidemics in past years, but I think that those of us whose perspective of this disease in Edinburgh is sufficiently wide, are inclined to consider that whilst it is still present, this epidemic began in Edinburgh in 1889-90.

Taking, however, its mortality curve at a later period, *i.e.*, at 1907, it will be seen that it then began to rise, and corresponding to some extent with C.S.M., it reached a maximum in 1908. It fell then, and corresponding closely with the C.S.M. curve, it maintained a minimum till 1914. Again, clearly corresponding with C.S.M., it rose till the middle of 1915-16, falling till 1917. It then shot up again during 1917 and 1918, keeping very high till 1919, although C.S.M. was maintaining its decline.

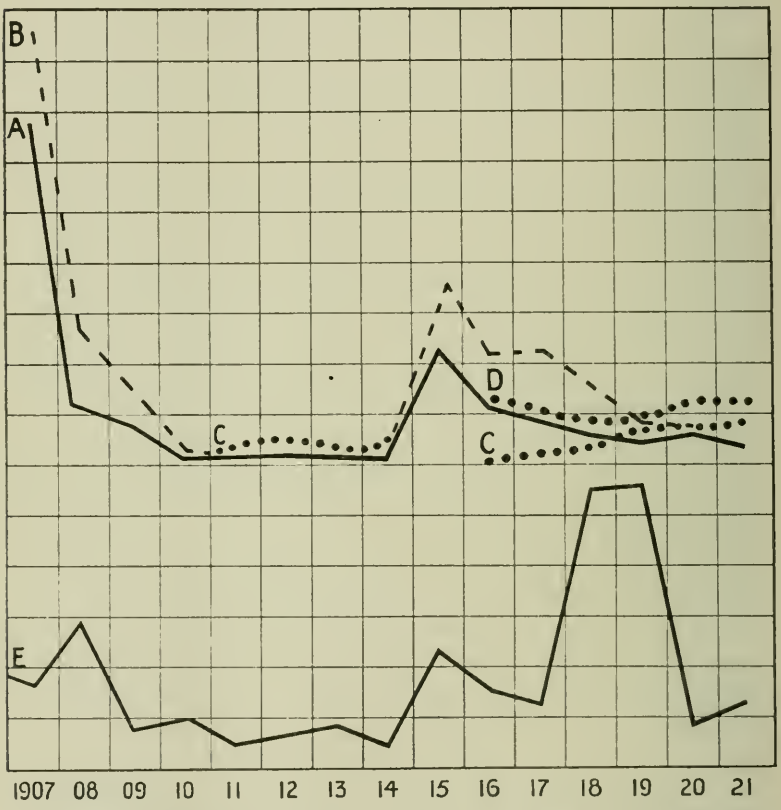
In this way some discrepancy between the influenza mortality curve and that of the C.S.M. becomes apparent after 1917, and the point which I would first indicate is that this discrepancy is really less than it seems. In the first place, the heights of the C.S.M. curve in 1914-15 and 1916 are higher than they ought really to be, owing, as has been already pointed out, to the large number of soldiers and sailors which the war had collected in and around Edinburgh, and the mortality among which adventitiously, as it were, increased the mortality registration figures.

But, in the second place, I would point out that there is reason for considering that the heights of the C.S.M. curve for 1917, 1918, 1919, and 1920 are too low. Epidemic encephalitis (C) made its appearance in the mortality statistics of Edinburgh in 1911, and increased to such an extent as to call forth notification in 1917, increasing still further till 1921. If now we add this encephalitis mortality to the C.S.M. mortality from 1916 onwards (D), it will be at once seen that the discrepancy between this curve and that of influenza largely disappears.

This implies naturally that epidemic C.S.M. and epidemic encephalitis are etiologically part and parcel of the same disease. I am one who holds that this is so, and that those two are practically one disease, and are related to influenza in the

same way as epidemics of pneumonia, pleuro-pneumonia, and empyema are. Let me point out evidence in favour of this view.

In the first place, it will be granted that encephalitis is practically always an associate of encephalic meningitis. We all know that, although in a typical C.S.M. case, the neck



In the chart the line A represents the mortality from C.S.M. in the period 1907 to 1921 The interrupted line B shows the notifications for the same period, and it will be observed that during 1911, 1912, 1913, and 1914 the notification and mortality lines are practically the same. The dotted line C, between 1916 and 1921, shows the mortality from epidemic encephalitis during those years. The dotted line C during the years 1911, 1912, 1913, and 1914, and the dotted line D from 1916 onwards show the mortality from C.S M. with that of epidemic encephalitis added. The line E shows the corresponding mortality from Influenza.

rigidity, the Kernig sign, and the results of lumbar puncture, will make the diagnosis of meningitis complete, yet we know also that in every epidemic of C.S.M. there occur cases in which the stupor, the hemiplegia, monoplegia, eye or face paralysis,

etc., are all present, and yet in which, by the absence of neck rigidity, of Kernig sign, and by the negative results of lumbar puncture, we have to admit that meningitis is not present. That is to say, we recognise that in such epidemics, encephalic toxemia and encephalitis can occur without meningitis.

But, secondly, we have further evidence in favour of this view. We all know that when a disease, which is always more or less with us in a sporadic form, takes on epidemic characters, the epidemic shows a rise, a maximum, and a fall, or decline. In the rise we observe, along with increase in the number of persons affected, a corresponding increase in its severity and mortality, at its height its frequency and mortality are at their maximum, whilst in the decline, we note progressive diminution alike in the number of persons affected, and in the severity of the disease in each individual case. Inasmuch then as it was in the decline periods of the C.S.M. epidemic, especially the later one, that encephalitis became most manifest, it follows that in this we have a piece of evidence in favour of the relationship of those two pathological conditions. More especially so when we reflect that encephalitis, though in all conscience, serious enough as a disease, is yet not so appallingly acute and fatal as C.S.M.

But, thirdly, it will be argued, if this predominance of encephalitis is detectable in the decline period of the C.S.M. epidemic, it should be also recognisable in the incline or rise period. That this was so, let me now point out.

At a meeting of this Society on 7th June 1905, I read a paper "On the occurrence recently in Edinburgh and neighbourhood of unusual forms of cerebro-spinal fever and intoxication resembling epidemic cerebro-spinal meningitis," in which I began with the following sentences. "Within the past fifteen years I have seen from time to time, as I daresay a good many others have, serious and often fatal cases of cerebro-spinal intoxication and fever, in which the ordinary causes of such symptoms could be excluded, and for the explanation of which, therefore, some less ordinary infective or toxic agency had to be thought of. Within the past few months it has been my experience to see in the Infirmary and elsewhere of such cases, a much larger proportion than usual." In illustration of such I detailed eight cases, but, for my present purpose, I shall quote only three of these in a condensed form.

Case I.—One day in May 1890, a number of boys belonging to the Edinburgh Industrial Brigade Home were having a holiday in the

country. Whilst they were all at play, one of them, a healthy-looking boy of 13, was discovered lying on the ground at the foot of a tree in a state of unconsciousness from which he could not be roused. He was conveyed home, and in the late afternoon I saw him. He was rather pale, and his pupils were dilated; pulse 80 per minute and rather feeble; his temperature was normal. From his companions, all I could ascertain was that he had complained of some headache in the early part of the day, and that it was most unlikely that he had fallen from the tree or had sustained any hurt. About 11 P.M. twitchings of the muscles of the face with some retraction of the head were noticed, and these continued at intervals till 1 A.M. when he died.

At the sectio, with the exception of some hyperæmia of the grey matter of the pons and medulla, all the organs were found quite healthy.

Case II.—On the 17th April 1905, a schoolboy, aged 8, was out with his companions in the street, watching a performing monkey, when he suddenly fell to the ground. His companions helped him home, and noted that he seemed to drag his left leg, and that he was crying out from pain in the head. On arriving home and being put to bed, he became dazed and partly unconscious. When roused, he complained of pain in the head, especially on its right side. The doctor on arriving found his temperature 98, pulse 88, and noted that the left side of the face, left leg and left arm seemed paretic. He had vomited once or twice, and the fæces and urine were being passed in bed. During the next three days, his condition remained much the same. At times he was restless and crying out, and complained very much of headache. The pupils were somewhat dilated. On the fourth day he was lumbar punctured, and 9 c.c. fluid withdrawn. It came away under considerable pressure, but was quite clear. This was followed by improvement, and though for some days he was very cross and sometimes obstreperous, he soon made a good recovery.

Case. III.—A woman, aged 48, who had always been a active and hard-working wife and mother, began to feel ill about the beginning of March 1905. She complained of feeling tired and of some headache, and it was noticed that, though she was still going about doing her home duties, she was dull and lethargic, not speaking so well, not walking so well, and forgetting things. The doctor who saw her found some paresis of the right face and arm, and to a slight extent also of the right leg, and advised that she should be kept in bed. On 9th March she complained of very severe headache, especially on the right side, vomiting came on, and she rapidly became dazed and difficult to rouse. Temperature and pulse remained normal, but urine and fæces were passed in bed. On 15th March a status epilepticus was noticed, the fits beginning at 2 P.M. and continuing

every few minutes till 6 P.M. On 19th March lumbar puncture was performed, and 9 c.c. fluid withdrawn, it showed no tension, and film and culture showed nothing abnormal. After the puncture no improvement showed, indeed, she became again restless and delirious. On 21st March lumbar puncture was again performed, and, under distinctly increased tension, 17 c.c. clear and normal fluid were withdrawn. After this she improved very much, and in about a week she was up and moving about in the ward. On 7th April, however, she was again not so well, complaining of a return of the headache. She went back to bed, and rapidly got worse. During the next few days she was in a state of stupor, with at times twitchings, and on 15th April, after violent twitchings of the right arm and leg, she died.

On post-mortem examination, beyond very intense hyperæmia of the grey matter at parts in the pons medulla and cord, nothing distinctive could be found.

Very soon after this date, June 1905, cases of definite cerebro-spinal meningitis were showing themselves in and around Edinburgh, and as I have already indicated, these increased so rapidly in number and severity, that in 1907 municipal notification and isolation was deemed proper and justifiable.

In recapitulation then of my subject at this stage, I would submit—that corresponding with a recrudescence of the influenza epidemic we had to recognise the onset of an epidemic of cerebro-spinal fever; that this epidemic was characterised in its stages of onset and rise by forms of encephalic intoxication and encephalitis; that as it increased in frequency and severity to its maximum, meningitic trouble more and more definitely supervened, and that with its decline those meningitic processes became gradually less and less marked, leaving encephalitis and encephalic intoxication as the predominant final characteristics.

But now, when we seek for facts which can strengthen the links of this chain of argument, we can, I think, easily find some other important considerations.

In the first place, we can readily understand how there should be a close connection between influenza and those forms of nerve trouble.

The nervous system is the system, a special concern of which is to radiate out to the other systems of the body a trophic or vitalising influence. Indeed it is only the truth to say that the nervous is to the other systems of the body what the sun is to organic life on the surface of the globe.

Here, however, the analogy ends, for unlike the sun, which with its vitalising rays, is constant unchanging and eternal, at any rate to the human mind, the nervous system, although the chief, is only one of the many systems of which a body is composed. It must, therefore, with all the other systems, share in the strains, struggles, and vicissitudes which life entails. That the energy of its vitalising radiations must vary correspondingly is evident, and it is also evident that there must be times, why and how we need not speculate, when this energy is so lowered that disease processes, ordinarily innoxious, become potent for harm, not only to one or any of the other tissues of the body, but to the nervous tissue itself. Among all such disease processes influenza stands pre-eminent, so that when we read of the old medical writers stating that influenza can "herald" in practically every disease that flesh is heir to, we can, with our present knowledge of disease organisms and their relations to living tissues, acknowledge these statements and grant to them a very large measure of truth.

But in special connection with our subject, a matter of importance is to discover whether or not in any of the older epidemics of influenza, a "heralding in" and intensifying of nervous maladies, characterised by symptoms, such as we have been seeing lately, has been observed by them. Of course those old writers had not the means of diagnosis which we now possess—neck rigidity, Kernig sign, reflex changes, lumbar puncture, with its chemical and cytological disturbances, were unknown to them — still a reference to their descriptions of influenza epidemics affords evidence that such cases of nerve disturbances were not wanting.

Graves, in his clinical lecture on influenza, delivered in 1836, states that the epidemic of 1834, whilst mainly affecting the respiratory organs, "carried off some very suddenly with cerebral symptoms." And again he writes: "In three cases . . . the attack terminated in a chain of symptoms bearing a close analogy to delirium tremens."

In the *Edinburgh Medical Journal* for 1848 there is a long excerpt from the Registrar-General's Reports for 1847, in which, after pointing out how the presence of influenza for that year had enormously increased the death rate from all other diseases, but specially pulmonary, it is stated :—

"There was, during the whole season, a great run of

hysterical, hypochondriacal, and nervous distempers, in short all the symptoms of relaxation. These symptoms were so high in some cases as to produce a sort of fatuity or madness, in which for some hours together they would be seized with a wandering of their senses, mistaking their common affairs, at the same time they had not any degree of fever to confine them to their beds."

Between 1851 and 1858 influenza was more or less epidemic, and Dr Parkes of London, who wrote the article on Influenza for Reynold's *System of Medicine* (published in 1866), was no doubt largely drawing on his own experience when he wrote as follows:—

"There is often great heaviness, sometimes torpor, and occasionally delirium. There is a general lowering in the acuteness of all the special senses, the spirits are low, mind weak, the nights restless, and this loss of sleep is not in relation to the fever, it is often seen in patients without fever." He further goes on to say: "The epidemic of 1712 was attended in Tübingen by great drowsiness, and in that outbreak the brain symptoms appear to have been unusually heavy. The extreme prostration of muscular strength is often a very early symptom, and in some epidemics has given almost a special character to the disease, the complete return of strength does not recur till after convalescence is far advanced."

In this way then I think there can be little doubt that although cerebro-spinal meningitis and encephalitis do not appear in the Registrar-General's Mortality Statistics until recent years, yet these morbid conditions have been occurring, associated with influenza, with marked frequency in long past times.

And now in conclusion to this part of my subject let me submit one further consideration.

Apropos of epidemics in general, the French physician Colin has stated: "It is the disease which constitutes the epidemic, not the epidemic the disease; the evil always remains the same, the number affected alone being increased." This implies, if our theory be correct, that encephalic intoxication and encephalitis cases must always be with us, in sporadic form, simply because they are, as it were, the rivulets which, during the epidemic, can come down, as it were, in spate.

What I wish now to emphasise is that these morbid conditions are not only always present among us, but are so in much greater proportion than is at present recognised. This

is simply because when any case of sudden loss of consciousness and hemiplegia comes before us, a diagnosis of cerebral hæmorrhage, cerebral thrombosis, or cerebral embolism looms in the medical mind far too largely and exclusively. I have always thought that doctors are too apt to regard a sudden catastrophe inside the skull just as a plumber regards a sudden catastrophe inside a home, that is to any, as due to a blocked pipe or a burst pipe. I could give you many examples of such, but I will content myself with *three*:—

Case I.—A young ploughman, aged 21, had been working all day in very hot weather, came home with severe headache and sickness and feeling very done up. Went to bed, and a few hours after was found unconscious, remained so for three days, and then found to have left hemiplegia. Had always been healthy, but gave an indefinite history of venereal disease eighteen months before. Specific thrombosis was diagnosed, but it was no doubt encephalitis.

Case II.—A girl of 19 had diphtheria in a somewhat mild form and recovered quickly, and after three weeks went out and walked about too much, came home complaining of headache and vomited, went to bed and rapidly became unconscious. After a few days recovered consciousness and right hemiplegia—face, arm, and leg—with aphasia were discovered, with later on some vision difficulty. Considerable improvement followed. At the time, 1896, embolism or thrombosis were thought of.

Case III.—A big, strong hefty man, of 58, who had always been well, although he had been rather liable to "flu," was in his shop one forenoon when he began to feel confused and giddy so that he went home to bed. Next morning was in a stuporous condition, and as the day wore on it was noticed that while this was getting worse he was not moving his right arm and leg so well. There was no albuminuria, but from his florid complexion, full pulse, and loud heart sounds cerebral hæmorrhage was suspected. Contrary to expectation, after a few days he began to recover, and this recovery was so pronounced that some four months after, not only was there no paralysis, but he was walking about busying himself with his work, his only complaint being that though he could see all right he could not read. Examination showed that it was his visual memory field that was at fault, and whether in this case the damage was in the lower parietal region or at the tip of the occipital lobe, it must be admitted that neither of those regions are regions in which hæmorrhage is likely to be the cause of the damage.

There can be no doubt then that encephalic intoxication and encephalitis are always with us in their less severe sporadic

forms, and we can also believe, I think, that associated with influenza they are apt to become epidemic, extraordinarily severe, and fatal. Further, we have also, I believe, grounds for considering that in their most severe epidemic forms meningitis is apt to supervene, and that this enormously increases their fatality.

But there is still another point which I wish to submit as regards influenza. If influenza can so intensify the powers for harm of the disease encephalitis, always with us, and ordinarily relatively mild as far as immediate danger to life is concerned, surely, as I suggested years ago, influenza can also act as regards the many long-enduring cerebro-spinal and nerve maladies which, in their chronic forms, are also always with us.

Clinically, there is much that seems in favour of this view, for we not infrequently see, associated with attacks of influenza and encephalitis, cases in which all the clinical features of a lateral or disseminated cerebro-spinal sclerosis or a paralysis-agitans become as developed in as many months as ordinarily, to make like downward progress, they would require years.

In connection with the subject of encephalic intoxication and inflammations, the influence of age is also one which presents considerable etiological interest, and I propose now to say a little about this.

Many years ago, bearing in my mind the dictum of the older medical writers that brain tubercle is the tubercle of infancy, abdominal tubercle that of boyhood and girlhood, and pulmonary tubercle that of adult life, I set myself to think out an explanation of this. The explanation which I adduced was that in a general way the resistance power of a tissue to disease-producing organisms is lessened about the stage when, in that tissue, growth has ceased and development begun. In this way, as the maximum growth of the encephalon is over by the third or fourth year, the maximum growth of chest about the twenty-first year, and the maximum growth of the abdominal viscera somewhere between those ages, we have in this physiological fact a logical enough explanation. I pointed out at the time that this law fitted in also as regards the ages at which tubercular disease showed itself in the various joints: hip, knee, ankle, shoulder, elbow, wrist, and as regards testicular and laryngeal tubercle. I regarded then the theory that, as growth meant increase in mass, while development meant change in structure, we might assume that at the

period when growth ceased, and development began, what had to be recognised as the exuberant vitality required for growth no longer existed. Applying now these considerations to the processes of growth and development of the nervous system, I would remind you that when a child is born, nature has seen to it that its organic life is assured by the existence in its spinal cord and medulla of completely elaborated and developed nerve mechanisms, the functions of which are to preside over organic life. These mechanisms are, of course, the simpler spinal reflexes, and the reflex and controlling centres for deglutition, digestion, secretion, circulation, respiration, etc.

It is otherwise, however, as regards the cerebrum proper, and as regards the cerebellum, pons, and other lower parts of the brain. When a child at birth passes into the world, it finds itself in a new environment. It has to acquire new sensory experiences, touch, temperature, pain, sight, hearing, taste, etc. It has to learn to know what the meanings of all these are, and it has to learn how to perform and co-ordinate its bodily movements in fit response to these myriad new sensory experiences. It learns all this as days, weeks, months, and years go by through its cerebral nerves and cerebrum, and having found that in the pons, cerebellum, basal ganglia, and other parts there is a partially prepared framework for the complex nerve mechanisms required, all these are gradually elaborated and developed.

In this way all the multitudinous and complex nerve mechanisms required for the evolution, physical, moral, and intellectual of the new being are channelled out, inter-connected, and developed from birth onwards.

If our theory is correct, therefore, it is not difficult to understand why a myelitis should tend to show itself at an earlier age than an encephalitis; and, moreover, it can give us an insight as to why the manifestations of an encephalitis, however protean they may be, should yet show variations according to the period of life of the person affected.

The question of a relation between influenza, cerebro-spinal meningitis, and encephalitis on the one hand, and acute anterior polio-myelitis on the other, is an interesting one, but I shall leave it alone in the meantime.

In conclusion, I would say that it is a great satisfaction to me to realise that in many ways the views which I have been

discussing with you as to the etiology of nervous diseases appear to be recommending themselves more and more to our profession as time goes on. My object to-night is to recommend them still more earnestly, and I trust that by demonstrating to you that they are views which were discussed carefully in this Society so many years ago, I can hope that this further recommendation is likely to be all the more favourably considered.

Discussion.

Dr Edwin Bramwell said that Dr James' communications to the Society had always been characterised by their originality, and although one might not agree with all his conclusions, one was always left with food for thought. Dr James was of the opinion, if the speaker had correctly understood him, that influenza had paved the way for the outbreaks of cerebro-spinal meningitis and encephalitis. Was it not possible, however, that some common factor had determined the incidence of these three affections in epidemic form? It would have been interesting to compare the curve for acute poliomyelitis had the material been available for this purpose. The mental and physical effects of a comparatively trivial influenzal infection were, as was generally recognised, "I think I must have had influenza, I feel so slack," was a remark with which we all are familiar. A case observed by the speaker was of interest, since it afforded demonstrable objective proof of the truth of such an assertion. A man, 78 years of age, had an apoplexy which resulted in a hemiplegia. When seen upon the following day the systolic blood pressure was 175. A fortnight later Dr Bramwell was again asked to see the patient, in view of the fact that a sudden fall in the blood pressure had occurred on the previous day. While after the attack of hemiplegia the blood pressure had remained consistently between 165 and 175, it had within twenty-four hours fallen suddenly to 110. Upon enquiry it was ascertained that three days before the speaker's second visit the patient had complained of some nasopharyngeal catarrh, and that the temperature, which had otherwise been subnormal, had at this time on two successive days risen to 99° and 100° F. respectively. The catarrhal symptoms and slight febrile disturbance would probably have passed without comment had not the nurse in attendance at the same time developed a typical influenza. It would consequently appear justifiable to assume that the patient had had an influenzal infection, which, although very mild in its obvious manifestations, had had a very pronounced effect upon the heart muscle. Dr Bramwell referred to another case which was, he thought, of considerable interest in relation to the influence of emotional disturbance as a factor in

determining or predisposing to an acute infection. A man of 45 was seen upon 20th April 1919. The patient, an individual of nervous temperament, had, his wife informed us, left home for his office upon the morning of 17th April in the best of health and excellent spirits. He expected to find a letter at the office informing him that he had received an appointment for which he had long been waiting. The same evening he reached home very depressed, in an emotional state, and complaining of a headache. He told his wife that he had lost the post, and she attributed his condition to the consequent disappointment; next day the headache persisted, and he vomited several times. When seen upon 20th April the patient was semicomatose, neck rigidity pronounced, the temperature was 102° F., and there was a profuse petechial rash. The clinical picture was typical of cerebrospinal meningitis. Within three or four days the patient was dead. While the possibility of coincidence cannot be denied, the facts certainly suggest that the depressing effect of a great disappointment had determined the onset of the acute infection. Dr Bramwell agreed with the reader of the paper that the relative frequency of encephalitis as a cause of hemiplegia was not generally recognised because of the customary tendency to ascribe an apoplexy to hæmorrhage, thrombosis, or embolism. With Dr James' remarks regarding disseminated sclerosis he was unable to agree. This disease was a definite entity, with a distinctive morbid anatomy and clinical features. He had never seen disseminated sclerosis as a sequel to acute epidemic encephalitis, although he was prepared to admit the possibility that an attack of acute encephalitis might accentuate the symptoms of disseminated sclerosis as influenza certainly did in some cases.

Dr Ker thought that the charts shown by Dr James were very suggestive of some connection between the diseases concerned. He doubted, however, whether the numbers of cases of encephalitis and of meningitis were sufficiently large to draw conclusions from. He thought there might be some common factor rendering persons more liable to diseases of this kind, even though the diseases were entirely distinct in themselves. Such a factor might be the epidemic constipation of the years concerned as laid down years ago by Sydenham. He alluded to the recent work on influenza by Cruikshank and others, and thought that Dr James' views were not unlike those expressed by Hamer.

HOUSE INFECTION IN CHOLERA AND CANCER.*

By Lieut.-Col. A. G. M'KENDRICK.

I TAKE the liberty of presenting to you this evening a problem which, whilst interesting in itself and in its applications, is illustrative of what is probably one of the most fundamental propositions of statistical mathematics.

Statistical mathematics, as you are aware, is the method by which one can, in a numerical manner, attack problems, which have to do with affections operating upon a community of individuals. Its methods were applied by Clerk Maxwell and Boltzman to the molecular theory of gases, and led to great advances in thermodynamics. They were also applied to chemistry, with the result that we have the laws of mass action which govern the phenomena of chemical dynamics. Although, with the discovery and realisation of the cell theory of Schwann, it became evident that physiology and medicine were fundamentally statistical sciences, it may be said that the methods of statistical mathematics have contributed little, if at all, to the advance of knowledge in this direction. I think there are two reasons for this, and these are closely related.

The first is that the non-mathematical vitalist shrinks from admitting that the law of chance is a law of order and beauty, which is, and must be, operative in all phenomena relating to communities whether they be living or dead. The second finds expression in the phrase that medicine is not an exact science.

I have stated that the law of chance is a law of order and beauty, which is operative in all the phenomena with which we, as medical men, have to deal. What I wish to impress is that whatever perturbations of that law may be present, the law itself is always operative. When apparent anomalies are met with they should not obviously be ascribed to any exceptional conditions or agencies, until the possibility that these anomalies are not merely the rare cases which occur in the normal operations of the law of chance has been excluded. Let me illustrate this point by considering the interaction of an emulsion of organisms with a dissolved disinfectant. Here we have two communities—the members of which collide with each other according to the law of chance. So long as the law of chance

* Read 6th December 1922.

admits of a single individual escaping collision, total disinfection cannot be attained. The larger the sample with which one has to deal, the greater will be the probability that there will exist in that sample the single individual which has escaped collision, and which causes all the trouble. In other words, outside chances can be demonstrated in large samples which cannot be demonstrated in small samples, and this because we are dealing with a suspension of discrete particles. This is exactly what occurs in practice. To disinfect a test-tube full of emulsion is an easy matter, to disinfect large bulks is extremely difficult. The natural tendency is to ascribe specially resistant properties to those organisms which have escaped collision; but disinfection follows, as it should, the law of mass action—or, in other words, the law of chance—and if we ascribe specially resistant properties to these long surviving microbes, we must, to be consistent, ascribe similar resistant properties to the molecules and ions which survive over comparatively long periods in ordinary chemical irreversible reactions.

We are met with the same problem in chemotherapy, when a drug is exhibited, which usually reaches the circulating blood stream in a very low concentration. The drug is expected to achieve complete sterilisation, and if it does not, the tendency is to put forward explanations depending upon varying strains with varying resistances—and this is done with a persistency which, without further investigation, is unfortunate.

I have stated that a second reason why the methods of statistical mathematics have not been applied to medical problems finds expression in the dictum that medicine is not an exact science. What the person who uses this phrase means I do not exactly know. Medicine is no doubt a very complicated science, but it is, or should be, exact, as every science which deals with representative facts must be. It has, however, peculiarities which are not usually met with in other sciences, and these have in part led to the accusation. The so-called exact sciences deal, as a rule, with the mean or average individual, and in the behaviour of the average individual the law which governs the process finds true and accurate expression. The medical sciences too often have to deal not with the average individual but with the extremely unusual individual—the individual who has experienced a phenomenal run of luck. In the vagaries of this individual the law underlying the process which is being investigated does not find true expression.

Disinfection is again an example. Here we are concerned with those individuals who, in the orderliness of the law of chance, have managed to escape a thousand collisions. We are not concerned with the individuals who succumbed in average time, in whose behaviour the underlying law finds true expression, but with the exceptional, with the one in thousands of millions, which ran a course which only one in thousands of millions could run.

We are met with the same difficulty in chemotherapy, in the search for minimal lethal doses, and indeed in all problems which aim at the eradication of living multiplying organisms whether in the body or in the test-tube.

There is another way in which medicine is not apparently an exact science, and this is essentially similar to that which I have just given. I have said that if we can observe the mean type of an affection amongst a community, then we have a true expression of the law or laws which govern the behaviour of that infection. But what if we cannot observe the mean type? What if our observation, or our experience as we call it, is outrageously selective? Let me give an example. We say that rabies is an incurable disease. But it was not until we had had recourse to animal experimentation that we could prove that the infection of an individual by the virus of rabies was an eminently curable condition. We defined rabies by its symptomatic picture, and we shut our eyes to the fact that, whilst the period of symptoms measures only two or three days, the course of the infection usually extends to six or eight weeks. The fact is that about 95 per cent. of those infected in the usual manner recover spontaneously, but as our definition of rabies is made dependent upon the symptomatic picture, we fix our attention on the remaining aberrant 5 per cent. who do not recover. The mystery of rabies lies not in the morbidity of the declared disease, but in the fact that the infecting virus produces no symptoms at all, until the patient is *in extremis*.

Again, it appears that about 97 per cent. of epidemics of influenza, arising from a single importation, die out before they have reached ten cases. We remember that such small epidemics are seldom reported—indeed the disease is not usually diagnosed until the epidemic has reached higher figures. And yet it is upon the remaining small percentage that we base all our ideas regarding influenza—and it is from the curves of these exceptional types that we seek to deduce our laws.

Would I go too far if I suggested that in these cases—those of rabies, of influenza, and might I add of cancer, and of many other diseases, we are forming our conceptions from observation and experience of types which may be as exceptional, and as remotely removed from the mean which expresses the underlying law, as were the organisms which survived disinfection over long periods, as are those individuals who have experienced a phenomenal run of luck.

In these respects then medicine is not an exact science; but let me impress upon you it becomes an exact science when we scrutinise it from the point of view which I have stated, and attack its problems by aid of the methods of statistical mathematics. To sum up this argument then. It seems to me that medicine is not in our hands an exact science, firstly and probably chiefly, because the observations upon which we base our reasoning are grossly unrepresentative; secondly, because we are forced so often, by the very nature of the problem, into the consideration of the grossly unusual; and thirdly, because the probabilities with which we have to deal are so small that they are mere "nuances," or almost imperceptible biases, only recognisable by means of massed statistical correlations.

The problem which I wish to describe to you this evening brings out some of these points, and shows how difficulties may be met and overcome.

An epidemic of cholera occurred in an Indian city. The total number of cases was 139, and these occurred amongst a population of tens of thousands. The infection was consequently minimal. The city received its water supply from a watershed, some fifty miles distant. The streams collected into a large lake. Contamination in transit was unlikely, the probable sources of water contamination were in the watershed area. It was calculated that the water took over eight days to pass from this area to the city. Now, in test-tube experiments, the vibrio dies out in two or three days, so it was argued that what was true in the case of the small bulk of water in the test-tube must be true for the large bulk of water in the lake and streams, and hence the epidemic could not be water-borne. I have already dealt with this fallacy.

The problem may be attacked as follows.* Let us consider

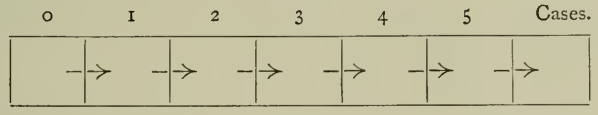
* See also M'Kendrick in *Science Progress*, 1914; *Proc. Lond. Math. Soc.*, 1914; *Indian Jour. Med. Res.*, 1915, 1916; and *Nature*, 1920.

house infection, and tabulate the house distribution of an epidemic at various intervals thus:—

Houses with :—	0 Case.	1 Case.	2 Cases.	3 Cases.
At first . . .	1000	...	..	...
Later . . .	990	9	1	...
Still later . .	980	17	2	1

The houses were at first free, then some picked up their first case. At a still later period some of these passed on to two or three cases, whilst others received their first case—and so on.

This may be generalised in a diagram.



Any particular house passes from one compartment to the next, and follows the path shown by the arrows, each arrow depicts the chance that a house may receive an infection and pass into the succeeding compartment.

Now, if a disease be distributed in a random manner, for example by water, these chances or arrows will all be of the same magnitude; but if the disease is spread by infection, then the arrows will tend to increase (for the chance of a fresh case occurring will tend to increase) with the number of cases which have already occurred in that house.

The problem is, then, to detect from observations whether the arrows do or do not increase with the number of cases.

Now those of you who are interested in chemistry will at once recognise that this is a problem of mass action, that is to say, a problem of probabilities. It is like a consecutive unimolecular chemical reaction where the stages are—

$$A \rightarrow B \rightarrow C \rightarrow D \rightarrow.$$

The solution presents no difficulties. If we denote the value of an arrow as being approximately $b\,(1 + a\,x)$, then all that is required is to find the value of a from the statistics. If it is positive, then the arrows will increase with x, the number of cases in the house. If it is zero, then the arrows will be constant, and the distribution is a random one. If negative, the arrows will decrease, and give evidence of some deterrent factor.

From the solution of the set of equations to which the diagram gives rise, we can also evaluate the total number of individuals (in this case of houses) which participated in the phenomenon. This is very important, because this total is often not exactly known, for example, in the case of water-borne infections, an area may have a number of water supplies only one of which may be contaminated.

In the case under consideration it was found that the arrows did not increase; and that, consequently, the distribution was a random one. The most probable random cause was the water supply. Chlorination was introduced, with the result that there followed a reduction in the mortality from intestinal diseases of a little over 70 per cent., as deduced from statistics contrasting the preceding period of five years with the five years during which chlorination was employed.

The figures were :—

	Observed.	Calculated.
Houses with 1 case . . .	129	128
„ 2 cases . . .	9	10
„ 3 cases . . .	1	1

The results of this experiment are not beyond criticism, but they afford an indication of the power of the method.

Here is a better example. The figures were from a village, and denote as before house infection. They were sent to me as an example of a contact epidemic.

	Observed.	Calculated.
Houses with 0 cases . . .	168	37
„ 1 case . . .	32	34
„ 2 cases . . .	16	16
„ 3 cases . . .	6	5
„ 4 cases . . .	1	1
Totals . .	223	93

The value a was negligibly small, so I reported that the epidemic was water-borne, but that there must be more than one well in the village, as the inhabitants of only 93 out of the 223 houses drew water from the infected source. The matter was inquired into. The village had two wells, and it was from only one of these that the houses in which cases occurred derived their water supply.

Here is a third case. A cholera epidemic broke out at Karachi. The local authorities considered it to be a contact

epidemic from pilgrim carriers. Colonel Hutchinson, now Sanitary Commissioner with the Government of India, went to investigate. He arrived in the forenoon, and by midday had personally visited a number of houses and collected statistics as above. He applied the method which I have described, and found that the distribution was a random one. Next morning the water supply was inspected. A gang of coolies was found working up to their waists in the water, mending leaks in the aqueduct. In their camp, which was close by, were cases of cholera. These operations were stopped, and the epidemic ceased forthwith.

Let me now give an example of house infection in cancer. Behla* found that in the town of Luckau in Hanover, two suburbs were heavily affected with cancer, whilst the remaining portions of the town were not. He publishes a map showing the case distribution in one of these suburbs. I am not concerned with why two suburbs were picked out by the disease, but with how the disease was distributed in the infected area.

Between the years 1875 and 1898, 73 cases occurred in the suburb which contained 120 houses. In two houses three cases occurred, and in one there were four cases. Referring to these he writes, this cannot be a matter of chance—"das kann kein zufall sein."

The figures are as follows :—

	Observed.	Calculated.
Houses with 0 cases . . .	64	65
„ 1 case . . .	43	40
„ 2 cases . . .	10	12
„ 3 cases . . .	2	2·5
„ 4 cases . . .	1	0·4
Totals . .	120	119·9

The value a was found to be $-0{\cdot}009$, which was taken as zero. The distribution was a random one.

If one includes earlier figures taken during the preceding twenty-five years, during which time diagnosis was not so accurate, then $a = -0{\cdot}19$, and the distribution was as follows :—

* Behla, *Cent. f. Bact.* (Orig.), 24. Abt. 1, 1898.

	Observed.	Calculated.
Houses with 0 cases . . .	46	46
„ 1 case . . .	48	48
„ 2 cases . . .	22	21
„ 3 cases . . .	3	4
„ 4 cases . . .	1	0·5
Totals . .	120	119·5

The agreement is, if anything, better.

In conclusion: Two of the examples of cholera house infection which I have shown you are cases of minimal infections. In these it would have been impossible to incriminate the water supply by bacteriological examination. In the first the conclusion arrived at was not in agreement with the view that vibrios can only survive for two or three days in water.

The points which I wish to emphasise are:—

1. That the infections were minimal.

2. That, as in the case of disinfection, the organisms which caused the epidemics were those utterly exceptional individuals which, by the law of chance, escaped dissolution or decay, though the chances against their doing so were immense. The law, as truly expressed in the behaviour of the average organism, was utterly remote from what actually happened. We were dealing with the last few survivors of a great body.

In the case of the cancer statistics there is no evidence of contact infection, or of infection resident in particular houses. This does not, of course, imply that the disease may not be of organismal origin, for neither in the cases of these cholera epidemics was there evidence of contagion.

As I said at the outset this problem of house infection was chosen on account of its illustrative properties. The method is generally applicable to all problems relating to the operations of affections of any kind or sort upon communities of any kind or sort. It is, if I may call it so, the first proposition of statistical mathematics. Once it is grasped, fields which apply to dead as well as living communities open up. From it can be deduced many laws of hydrodynamics and diffusion, of chemical processes of all sorts. In our own science of medicine we can deal with phagocytosis, agglutination, and any problems which relate to changes of state. In public health we can measure the degrees of immunity produced by diseases, the effects of treatment, the epidemicity of diseases—we can

differentiate between relapses and fresh infections, between importation and recrudescence. Many are the fields which open out before us. I have described only one of these.

Discussion.

The President (Sir Robert Philip) congratulated the Society on the communication to which they had listened. Colonel M'Kendrick had proved himself an able exponent of mathematical methods in relation to numerous medical problems. The present luminous statement was an excellent example of the value and nicety of mathematical calculation in tracing the causal and conditioning factors of disease.

Professor Russell said he had listened with much pleasure to Colonel M'Kendrick's communication, and admired the manner in which he had presented it. He had to acknowledge ignorance of the "methods of statistical mathematics." In medicine, however, statistics were used, as in the age incidence in certain diseases; averages based on these were also in use; but in the practice of medicine, where you had to deal with the individual case, both statistics and averages could be seriously misleading. Colonel M'Kendrick had referred to cancer. Statistics and averages showed cancer to be a malady of the later half of life, and so much had this belief dominated medical thought that, when he diagnosed stomach cancer in early adult life, the question put was, "Would you expect it?" In this way an early diagnosis was frequently missed. Again there was tuberculosis; here also there was an age incidence gleaned from statistics, but that did not help when, in a patient of sixty or seventy years of age, you were faced with the question of pulmonary tubercle. He might take one more example of averages. In so-called "blood-pressure," many doctors thought that raising of it was a normal consequence of advancing years, and there was an average adopted by some, of adding 1 mm. to 100 or 120 mm. for each year the individual had lived. There were no extensive statistics, but he had seen many persons up to and above eighty years of age who had no rise of "blood-pressure," and never had. These persons might be in the minority, but his contention was that the minority was the normal, and that normality was health. He had no doubt Colonel M'Kendrick could deal with these matters from the standpoint of statistical mathematics, although he could not. In practical medicine we had to deal with individuals in whom the personal factor was infinitely variable, and this upset any attempt at diagnosis by statistics or by age incidence. The chemico-vital equation or constitution, which was so variable, was an outstanding factor in many, if not in all the morbid conditions which emerged as life was prolonged, and with which physicians had to deal.

ARTIFICIAL PNEUMOTHORAX IN THE TREATMENT OF PULMONARY TUBERCULOSIS.*

By IAN STRUTHERS STEWART.

Dr IAN STRUTHERS STEWART gave a demonstration of a series of cases of pulmonary tuberculosis treated by artificial pneumothorax, illustrated by lantern slides made from X-ray photographs.

He showed the Vere-Pearson-Lillingston apparatus, and demonstrated the method of use and the technique of the induction and refills. Following this the indications and contra-indications were discussed. The question of the refills and the interval between the refills with the best intrapleural pressure was then brought up. The various complications and the best methods of dealing with them were reviewed. After this thirty-five lantern slides were exhibited on the screen, showing various types of pulmonary lesion and the condition before and after treatment by collapse.

In summing up, Dr Stewart said he had treated twenty-two cases in the past eighteen months, and of these twenty are alive and two are dead. In the two fatal cases artificial pneumothorax was only induced as a forlorn hope. Of the twenty alive nine developed fluid at some stage of the treatment, and of those two developed empyema, one tuberculous and the other septic. Five of the twenty cases were complicated by tuberculous laryngitis, in four this condition became quiescent, and latterly healed after the affected lung had been collapsed.

DISCUSSION.

The President, in thanking Dr Stewart for his demonstration, reminded the Society that the method of artificial pneumothorax was of much older date than was commonly stated, and had its origin in Britain. James Carson of Liverpool, in recommending the method in 1821, advanced very much the same indications for its practice as had been given by the speaker. It was not Carson's fault that the method had not been more generally adopted.

The significance of collapse of the lung in obdurate cases of persistent toxæmia, and in cases of recurrent, severe hæmorrhage, was freely admitted. It was in practice more difficult to say when the case was not going to benefit sufficiently by other methods. Dr Stewart had spoken of waiting six months. There could be no

* Read 6th December 1922.

arbitrary time limit. Each case was necessarily judged on its own merits. If a patient was advancing steadily—even if slowly—towards cicatrisation and disintoxication, it was generally wise to let well alone.

It was only right to make it clear to the patient that a pneumothorax line of treatment was a *prolonged* one. Four years had been cited as sometimes necessary. Certain other satisfactory lines of treatment were apt to be turned down as failures, unless results were obtained within much shorter periods. At the best, the effective arrest of tuberculosis required much time. Collapse therapy should he reserved for a limited, well-defined group of cases which, on sufficient trial by other methods, failed to respond adequately.

Professor Gulland expressed his personal gratitude to Dr Struthers Stewart for his most interesting paper, and also voiced his admiration of the studious fairness with which he reported both his good and bad results. The fact that he had so few accidents of any kind, showed the perfection of his technique and the care he exercised—not everyone had been so fortunate. The only point to which one could take exception was his statement that the natural end of pleurisy with effusion was bronchiectasis and septicæmia. The general experience was that these cases do exceedingly well with ordinary methods, and comparatively rarely proceed to further involvement of the lung.

Professor Meakins and Dr Davies pointed out that whatever gas be injected into the pleura it would eventually come into equilibrium with the dissolved gases of the capillaries. This equilibrium would cause an initial increase in the volume of the pneumothorax, owing to the rapid diffusion of carbon dioxide into the cavity.

From a consideration of the physiology of respiratory function, it can readily be seen that treatment by artificial pneumothorax would have a beneficial effect. In any case with extensive lesions it appears probable that in certain areas of the lungs the ventilation would be deficient, although the pulmonary blood-supply would not be correspondingly diminished. The result would be that the mixed blood returning to the left side of the heart would be deficient in oxygen. The collapse of one lung would almost completely abolish the pulmonary circulation of that side, while the ventilation of the uncollapsed lung would be doubled, thus ensuring a more uniform distribution of air.

These considerations have been borne out by some recent and as yet unpublished work of Dr Dautrebande of Brussels. This observer found no evidence of disturbed respiratory function in patients with early localised lesions. In cases with extensive lesions, however, there was definite evidence of deficient ventilation and stagnation of air in portions of the lungs. Moreover, examination of the gases of the arterial blood disclosed the fact that there was definite oxygen

deficiency together with carbon dioxide retention. These conditions cleared up after the establishment of artificial pneumothorax. In addition there was great improvement in general health, diminished expectoration, and increase in the hæmoglobin percentage.

Dr Davies asked Dr Stewart whether, in his experience, artificial pneumothorax was followed by an increased incidence of miliary tuberculosis and tuberculous meningitis.

Dr John Stevens asked whether any other treatment was employed concurrently with that by artificial pneumothorax. He suggested that the beneficial results obtained by artificial pneumothorax were explicable, at least in part, on Hilton's principle of rest to the damaged organ.

Dr Savy suggested that the so-called pleural shock was in the majority of cases due to the introduction of gas into a blood-vessel. One heard very little about this alarming symptom before the introduction of pneumothorax treatment. He had never seen it in any of his own cases. He regarded high intrapleural pressure as very dangerous. It was probably one of the causes of very common complication of pleural effusion. In cases with marked systematic intoxication or with obvious adhesions, it was advisable not to leave a positive pressure of more than 1 or 2 cubic centimetres until the lung was well collapsed.

He did not agree with Dr Stewart in regard to the replacement of pleural effusion with gas. If there was no evidence of pressure symptoms or of pus formation it was better not to interfere too much.

Dr Guy remarked that while he agreed with the speaker regarding the simplicity of the operation, he desired to point out that there were always risks of air-embolism or pleural shock. In one of his own cases a colleague had been doing a refill, the patient died with tragic suddenness. Another great difficulty was the correct procedure to adopt in cases where the pleural cavity was filled with effusion. In his experience such cases could go on for months without apparent change. While there were many abstruse physiological points which seemed to be against the procedure of pneumothorax, still his experience was to regard the operation with increasing favour.

PRIVATE BUSINESS.

Meeting—6th December 1922.

The following were elected Members of the Society:—Charles G. Lambie, M.B., Ch.B., M.R.C.P.E.; William T. Gardiner, M.C., M.B., Ch.B., F.R.C.S.E.; William G. Liston, C.I.E., M.D., Lieut-Col. I.M.S.; A. Humefulhbech, M.B., Ch.B.; Arthur W. S. Christie, M.B., Ch.B., F.R.C.S.E.; William A. Alexander, M.B., Ch.B.; James N. J. Hartley, M.B., Ch.B., F.R.C.S. Edin. and Eng.; John W. L. Spence, M.B., C.M.

PRINCIPLES OF BONE GRAFT SURGERY.*

By ALBERT E. MORISON, M.B., F.R.C.S.

In opening my subject I wish to say that while these principles of treating un-united fractures of bone may apply to civil surgery, the greater part of my experience has been gained by dealing with war wounds. The late war has given surgeons an opportunity of deciding upon some definite principles which govern the grafting of bone and the processes that take place for their repair and consolidation. Much of this work is materially different from that in civil practice, because as a rule there is loss of a less or greater amount of bone; and the result is either the formation of a false joint or a wide interval between the ends of the bone to be dealt with. Two great factors are present which are seldom encountered in non-military surgery. These are:—

1. Latent sepsis. 2. Scar tissue.

1. **Latent Sepsis.**—In a very large proportion of these cases with which we are dealing sepsis is present, and though in most instances the wound has healed and remained perfectly sound as far as outward appearances are concerned, it is often still potentially septic. We recognise how disastrously operative interference may terminate in many of these cases, by setting free organisms which have been incarcerated in the scar tissue and which when thus liberated infect the whole wound. We therefore avoid any bone graft operation until assured that latent sepsis is absent. Many methods have been suggested to overcome this. Some authorities advise that every operation should be done in two stages—first removal of the scar tissue which would light up any sepsis that might exist and allow of suitable treatment, and then at a later stage, proceed to perform the bone grafting part of the operation. Others recommend postponement of any operation for six months or longer after the wound has soundly healed. Experience has, however, shown no such definite criterion of safety in the time factor.

The following case demonstrates the truth of this:—

Case I.—S. M., un-united fracture of humerus.

History—Was wounded in right upper arm, September 1918, and the humerus broken. It did not unite and was plated in November

* Read 17th January 1923.

1918. The wound became septic and the plate was removed in three months.

8.6.20—He was admitted into the Sutherland War Pensions Hospital. The humerus was un-united below the deltoid insertion. There is a scar about 5 inches long on outer aspect of the arm and adherent to the bone. X-rays shows the ends of the bones atrophied. Radiant heat was ordered. After each application he complains of a toothachy, throbbing pain in the arm.

FIG. 1. T. J.—*Before Operation*—Note lower ends of radius and ulna ankylosed. Small fragment upper end of radius.

30.7.20—First operation. Excision of scar. The scar was excised, the skin under cut, washed with spirit—bipped and closed. Healed per primam. Radiant heat again applied gave the same throbbing deep pain, but only to a slight degree. No rise of temperature—no reaction in the skin.

24.11.20—Second operation. Exploration of bone. The scar was opened up and the bone exposed. The upper fragment was soft and pulpy and looked unhealthy. In the lower end was a small sinus leading into the medulla, and on opening this up a small

granuloma with a tiny sequestrum was found. The granulation tissue was sent to the bacteriologist who found staphylococci, two years after the wound had healed.

The bone graft operation was of course postponed.

We must therefore not rely on this uncertainty for the final obliteration of latent sepsis.

The method which I have for several years adopted both in this type of case and in wounds of the brain, is the test of radiant heat (see *Lancet*, 13th April 1918).

FIG. 2. T. J.—*After Operation*—Radius and ulna separated. Two ends of ulna refreshed with chisel and plated. Double cricket-bat graft into radius. Arm put up in full supination. Good functional result.

It is a very reliable and constant guide, and by its use we were able to discover latent sepsis in 10 per cent. of all our cases. No case in which it was properly applied failed to respond if latent sepsis were present. In a few cases the test appeared to deceive us, but on making inquiries we found that instead of a 2000 c.p. lamp having been used, as this had been broken, a 250 c.p. one was used in its place. A return to the higher powered lamp showed that no case failed to respond.

The method is to apply radiant heat from a 2000 c.p. lamp to the seat of injury for a period of eight or ten days, with a

daily exposure of five minutes increasing to fifteen minutes. Should there be any reaction, such as toothachy, throbbing pain in the scar, redness and slight swelling, the application of heat should be stopped for a few days and again re-administered in a similar manner at the end of that time. If the scar again flares, the wound should be opened by excision of the skin scar. The incision is carried down to the bones, the intervening scar tissue excised, and the ends of the bones are explored for any hidden focus of infection. The wound is washed out with alcohol, bipped and closed with silkworm sutures. As soon as it has healed, another course of radiant heat is ordered, and if a negative result follows, the second stage of the operation—insertion of the bone graft—is proceeded with. Under this régime, there has been a disappearance of cases of sepsis such as previously were brought into activity by the operation. Should a definite focus of infection be found, a culture is taken from it and an autogenous vaccine made and administered by a skilled bacteriologist.

I am satisfied that some of these cases of secondary sepsis are due to a hæmatogenous infection of the graft. Such a case is the following, and it is in this type of case that an autogenous vaccine is indicated, and may be of special value.

Case II.—T. F., un-united fracture of right radius.

History—Was wounded in 1917.

C.O.A.—Admitted into the Sunderland War Hospital on 31st October 1919. There is great deformity of the right forearm. The hand is drawn to the right, and there is a scar over the lower end of the radius, adherent to the bone. About half an inch of bone is missing, and the upper end of lower fragment is touching the ulna. Radiant heat ordered—no reaction.

2.12.19—Skin scar excised and arm rectified from radial flexion. No reaction to radiant heat.

21.4.20—Operation. Bone graft into radius. Wound healed per primam.

12.5.20—X-rays shows good alignment and new bone being thrown out round the graft.

27.9.20—Discharged with good use of arm.

10.10.20—Readmitted suffering from acute pneumonia at left base, following influenza. Is very ill. Sputum found to contain pneumococci.

19.10.20—Complains of pain in right forearm where the bone graft was inserted into the radius. Temperature normal. Arm swollen and red. Incised under a local anæsthesia, and a quantity of green

pus evacuated. Bacteriological examination stated it was pneumococcal and a vaccine was prepared from it.

16.11.20—Developed an inter-lobar empyema. Pus evacuated.

14.4.21—Graft found partially necrosed and removed.

16.6.22—A subsequent graft gave a good result.

2. **Scar Tissue.**—This is present to a less or greater degree in most of the cases due to war wounds. It has been for me a recognised rule in bone graft surgery that before proceeding to transplant bone, the tissue which is to envelop and cover the graft must not be scar. All skin scars are therefore excised, but the deeper scar tissue need not be removed, except that which intervenes between and is attached to the two ends of the bone. Care is essential in removing the deeper scars. The anatomical relations of vessels, nerves, etc., have been altered by contraction of this tissue, and may be injured in the attempt to remove all of the unhealthy tissue.

In some instances it may be necessary to *excise* a large area of *skin* and cover in the gap by a sliding or tubular or pedicle graft from some other part, and later when healthy mobile skin covers the limb, proceed to insert the bone graft. Another point of great importance is that no bone graft operation should be undertaken until there is *free voluntary movement* of the joints and tendons of the injured limb. This is essential if a successful functional result be hoped for. Remember that every limb upon which a bone graft operation has to be done requires immobilisation for a period varying from six to twelve weeks and this will be evident—stiffness, deformities, and disabilities of the joints and muscles must as far as possible be rectified before the final operation of bone grafting is attempted.

One point more—the patient should, as far as possible, have become *accustomed to the position* in which his limb will be fixed after the operation by a preliminary application of whatever retentive apparatus may require to be worn after the operation —*e.g.* in bone graft operations on the upper third of the humerus where an "out-rigger" splint is generally applied, it should be worn for some days and nights prior to the operation.

The Nature of the Graft.—Whatever the nature of the graft may be, the larger it is within reasonable limits, the greater the chance of ultimate success. As a rule I have obtained it from the antero-internal surface of the tibia, but have also utilised the fibula and the crest and dorsum of the ilium. It happens more frequently than one cares to note,

that if the crest of the tibia is removed, fracture of the leg follows. This has happened in two of my cases, and I therefore now avoid taking it away.

The *length* of the graft should be liberal. The longer the contact between it and the recipient bone, the greater the probability of success in the result. However small the intervening gap between the ends of the bone may be, the contact area between the graft and the recipient bone should not be less than 1 inch at each end, and the rule I now follow is to make the graft three times the length of the space to be bridged—*i.e.*, a gap of 2 inches would require a 6-inch graft.

Fig. 3. J. W. M.—Un-united fracture radius.

Periosteum is taken with the graft and undisturbed as far as possible, except where an intra-medullary graft is used, in which case the periosteum is stripped off the endosteal portion. The length of the graft is measured with a pair of compasses after the recipient bone and its bed have been prepared. The length and breadth and shape of the graft are then marked out on the tibia by incising the periosteum down to the bone longitudinally, and transversely with a knife. An Albee's saw with a single blade cuts the graft, while cold normal saline solution is played on the rotating saw during its use. In the case of an inlay graft, the bone is divided in a bevelled manner by holding the saw blade on the slant till it penetrates the medullary cavity. This shape of the graft adapts itself more readily to the recipient bone, allows of a wider

and larger graft being taken, and of a longer and more accurate apposition of the graft to its host.

Types of Graft.—The kind of graft I have been in the habit of using varies greatly with the condition of the recipient bone and the position in the bone for which it is required.

1. *The inlay graft*, made use of as a rule when the missing piece of bone is near the centre of the shaft, and when the requirement laid down in making the graft can be fulfilled—*i.e.*, when the graft can be made three times the length of the bridging portion.

Fig. 4. J. W. M.—Double cricket-bat graft fixed with split pin. Split pin removed later. Good result.

2. *The inlay intra-medullary*, made use of as a rule in the proximity of a joint where one portion of the recipient bone is short, and consists largely of cancellous bone. The intra-medullary portion is driven into the cancellous bone—*e.g.*, upper end of humerus, lower end of radius, etc., and the inlay fitted into a prepared surface on the longer fragment of the host bone.

3. *The "cricket-bat" intra-medullary graft*, where the bridging portion is short and where strength and stability are required. The principle of this graft is that two pieces of bone the same length are cut and shaped like a cricket-bat with a handle and blade. The two bats are taken from the tibia and shaped with square handles, wider blades, and rectangular shoulders. The periosteum is removed from the handles, and each is driven into the medullary cavity of the

recipient bone previously drilled out with a drill, and in such a way that when in position the front of the blades—*i.e.*, the medullary portion, will be in contact and the periosteal surfaces away from one another. The shoulders of the bats must come into close touch with the ends of the recipient bone. The two blades are then fixed together with two split pins, passed through both blades. It does not matter, indeed it is rather an advantage if the recipient bone splits a little while the handle of the bat is being driven into it. One or two encircling ligatures of catgut will prevent further splitting. This makes an excellent strong graft and its advantages are :—

(1) The square handle in the round hole prevents rotation of the graft ; the square also leaves gaps in the circle for lymph lavage and blood supply ;

(2) Early movement (in three or four weeks) is possible with the resulting rapid formation of new bone ;

(3) A strong bridging graft is obtained—this graft is used in fractures of the radius in its upper third, in grafting into the clavicle, in un-united fracture of the humerus within 3 inches of its lower end.

4. *The "cricket-bail" graft* has the drawback that it is difficult or even impossible to introduce unless the terminal ends of the bat are short ; it allows of too much play on the ends of the graft, and too short contact with the recipient bone. I have never made use of it.

5. *The "stepping" operation* as in non-union of the humerus often gives good osseous union, but as often entirely fails. It, however, produces a considerable amount of shortening of the bone and consequent weakening of the muscles of the limb. I have never employed it for this reason, but have seen several cases where, owing to the shortening of the biceps, brachialis, and triceps, loss of "tone" was sufficiently marked to cause disability of the arm.

6. *The "wedge-shaped" graft*, as used by gardeners in grafting trees, may be of service in cases where the ends of the recipient bone are attenuated and thin, and any other form of graft difficult on account of the narrowness of the bones. The two ends of the host bone are split, and the wedge-shaped ends of the graft inserted into the gaps.

Method of fixing the graft.—Whatever the means of fixation, accurate apposition and prolonged immobilisation between

the recipient and the bone graft are necessary to ensure the speediest and best results.

1. *The ideal method*, all surgeons are agreed I think, *is by the use of some absorbable material* which will not require subsequent removal, *e.g.*, Kangaroo tendon, 40-day chromic catgut, strips of fascia lata or tendon, etc.

This, however, has the great disadvantage that prolonged immobilisation of the limb with the joints above and below the grafted bone is essential to success. The enforced rest prevents free movements of the joints and muscles, and delays union and ossification of the graft. It also tends to decalcification of all the bones of the limb, and so increases the tendency to non-union and fracture of the graft.

2. *Wire sutures*—preferably phosphor-bronze or piano-wire encircling both bones—hold the apposed bones more rigid and firm, but have the drawback that they frequently break, allowing of a separation between the bones; and their use also leads to absorption of the bones round which they are fastened, with consequent loosening of the graft. In many instances, too, they have to be removed at a later date.

3. *Split pins*, *bolts*, *metal* (*not joiners'*) *screws* hold the bones more rigidly and accurately in apposition than any other form of fixation, and so allow of earlier after-treatment and mobilisation of the limb; their presence leads to some irritation and so a deposit of new bone. All, however, have the disadvantage (it is not a negligible one) that sooner or later they may require to be removed. Their advantages so greatly to my mind outweigh this drawback, that I do not hesitate to make use of them, especially in difficult cases.

4. *Bone screws and bone pegs* are of the greatest service in ordinary fractures where there is no loss of bone which requires bridging, but have not in my opinion any place in bone graft surgery where so much depends on stability and rigidity. In some of my earlier cases I tried a combination of bone pegs with a nick at each end, into which an encircling catgut suture was passed, but obtained no better results than with the plain absorbable non-rigid suture.

5. *Metal bone plates*, combined with bone grafts. This method though open to the many disadvantages caused by the insertion of a foreign body has still, I think, a place in many cases. These are chiefly instances of non-union of the femur, humerus, clavicle, tibia, where without some comprehensive

form of outward application for complete immobilisation, non-union is so apt to occur. In all these instances, prolonged rest and the wearing of some cumbersome apparatus are necessary unless one resorts to such an efficient method of internal splinting as the application of a suitable metal plate. It means additional comfort to the patient in that he is not kept so long immobilised, generally and locally; it ensures a successful issue more frequently than where a bone graft alone has been inserted, and its only disadvantage is that the plate may require removal sooner or later. The application of a metal plate to the un-united bone before inserting the bone graft renders the

FIG. 5. P. R.—Un-united fracture tibia. *First Operation*—Pedicle graft from calf of opposite leg.

process of implantation and fixation of the graft much simpler, and so occupies less time in difficult cases.

It should now be unnecessary to add that in un-united fracture of a bone with formation of a false joint, union will never take place by simply cutting away the intervening fibrous tissue, and then applying a metal plate. So many cases, however, have come under my notice that I mention this merely to condemn it as useless and bad surgery.

Technique of the Operation.—As soon as the preliminaries to which I have already referred have been attended to, the patient is prepared for the operation of bone grafting. He is kept in bed the whole of the previous day, an enema consisting of a quart or more of normal saline solution is given to flush

out the colon, but no aperient administered. His diet should be light with plenty of liquids.

The evening preceding the operation the limb to be operated on and that from which the graft is to be taken are washed with spirit soap and hot water, dried, and enveloped in gauze soaked in methylated spirit and wrapped in a dry sterile towel. The spirit gauze is renewed the following morning two hours prior to the operation and replaced by fresh dressings of the same. On the operating table the parts are scrubbed with Harrington's solution, followed by methylated

FIG. 6. P. R.—*After Operation*—Inlay medullary graft fixed with split pin. Good result.

spirit, the portion of the limb below the operation area—foot or hand—is covered with a double layer of sterile towelling which is fixed on with a sterile bandage. This allows of the limb being readily manipulated during the operation, if necessary, without exposure of the skin.

The incision through the skin, which should be extraordinarily long to obtain the necessary exposure without undue injury to the underlying tissues, is made a short distance from where the deep layers are divided, so that it is not directly over the site where the graft is to be applied. The skin and subcutaneous tissues are freed on either side and the skin surface covered over by cloths of butter muslin fixed in position

to the edges of the wound with Michel's clips. From first to last no hand contact with the wound is allowed. Swabbing is done by gauze mops held in dissecting forceps; all ligatures are tied with forceps, so that even the gloved hand does not touch anything that is introduced into the wound, etc.

The ends of the bone are exposed by dissection through the deeper tissues and the gap in the bone laid bare. Fibrous tissue between the bony ends is removed, and the periosteum separated off the exposed bone for the necessary distance above and below the gap. The host bone must be disturbed as little as possible from its periosteal and muscular bed. It interferes, I think, with the bone repair to free the bone throughout its whole circumference. The ends of the bone are generally found to be sclerosed and fibrous, and this is not a good surface upon which to imbed a graft, as its osteogenetic value is very small. It should therefore be removed, but may be utilised to lay beneath the new bridge of bone which stretches across the space between the two ends, by sawing it partly across and bending down into position the fragments still adhering to the under surface of the bone by periosteum and fibrous tissue. The next step of the operation is the preparation of the recipient bone for the graft and depends upon the nature of the latter—whether inlay or intra-medullary, or both. These are prepared by an Albee's saw or drill. The length of the graft required is next measured by a pair of compasses. If sutures are to be employed to hold the graft in position, they are now passed under the recipient bone, generally three or four on each side about half an inch apart. The wound is then packed with hot moist gauze and covered with a dry sterile towel until the graft is obtained from the tibia.

A curved incision is made over the front of the leg, and a semi-lunar flap of skin reflected inwards. Bleeding points are caught with forceps and the skin is shut off with gauze. The importance of infection of the skin is well illustrated by the following case:—

Case III.—Pens. J. T., admitted into the Sunderland War Hospital under my care with an old G.S.W. of the left forearm, from which about 4 inches of the ulna was missing. The skin scar was very adherent to the underlying tissues. After a course of radiant heat it was excised, the marginal skin underpinned, and the two edges were easily apposed and brought together with subcutaneous sutures of catgut and Michel's clips. The wound healed per primam. In

fourteen days the bone graft operation was undertaken. While preparing the leg with the patient anæsthetised, a spot of psoriasis to which my attention had previously not been drawn was noticed on the front of the leg, but not in the line of the proposed skin incision. It was treated with pure carbolic acid, and as soon as the skin incision was made, the skin surface was covered over with butter muslin cloths. The operation was then completed. The leg became acutely septic, and for some time the patient was very ill. Staphylococci was found in the pus. The forearm wound healed without any trouble, and the result as far as the bone graft was concerned was all that could be desired.

The dimensions of the required graft are marked out on the antero-internal surface of the tibia by incisions into the periosteum, and the graft is cut with an Albee's saw. To prevent the bone from splitting at its upper and lower ends, I generally drill two or three holes at each end. The whole thickness of the bone into the medulla is taken. Any further shaping of the removed bone is then made with an electric saw or bone-nibbling forceps. The bone graft when loosened should be held in two efficient forceps to prevent it from falling during its transplantation. The packing is removed from the original wound and the graft laid into the prepared bed, and while the ligatures are being tied, the two bony surfaces of the recipient bone and graft are firmly apposed with a pair of sequestrum forceps.

If split pins, etc., are used, the bones are drilled *in situ*. In some cases where a metal bone plate is applied, it is fixed in position on the bone before the bed is made for the inlay graft. In other instances, the plate is laid over the graft and screws are passed into it to fix the graft and them into the recipient bone. In recent cases I have, in addition to preserving the ends of the host bone, packed round the ends and bone graft, bone dust taken from the tibia in hopes of expediting osteogenesis and preventing fracture of the graft.

Fracture of the Graft.—It sometimes happens that after a few weeks a fracture of the graft occurs, and its seat is generally at the proximal end at the junction of the two bones. This may be attributed to two causes :—

1. On examining such a specimen one finds that a considerable amount of lacunar absorption has taken place at this spot, owing to the penetration of new blood vessels into the graft, with a corresponding weakness and thinning.

2. Decalcification of the graft also takes place throughout its whole extent, though much more slowly where it is not in contact with the recipient bone. This is well seen in cases of transplantation of a tibial graft into the skull for bony defects in the cranium. In time, however, the graft again becomes more dense, as seen by the X-rays, showing that lime salts have again been deposited into the graft bone. This leads one to doubt whether absorption of the whole graft and its substitution by new bone does take place. Is it not rather that in the vicinity of contact of the two bones (*i.e.* the recipient and the graft), be the graft inlay or intra-medullary, union of the two bones (just as in a fracture) takes place by cartilage primarily, with the inevitable lacunar absorption by the penetration of new vessels from host to graft at the points of contact; that later ossification of these cartilage cells occurs with resulting firm union of the two bones? I have been led to this conclusion by the examination of several bone grafts of tibia into the skull that have fallen into my hands after periods varying from two to sixteen months following operation; by repeated and frequent comparison of the grafts as demonstrated by X-ray photographs, and by the fact (to which further reference will be made later) that if firm and accurate apposition and immobilisation be made between the graft and the host bone, so that early active and passive movements of the *whole* limb are possible, fracture of the graft occurs less frequently because of the earlier and more rapid calcification of the newly deposited cartilage cells.

This leads to a consideration of the *after-treatment* of these cases.

The limb is immobilised as a rule with plaster of Paris splints and fixed in the most suitable position. It is undisturbed for from fourteen to twenty-one days. At the end of this period the splint is taken off; the wound, which should be soundly healed, is dressed, and the clips or stitches removed and an X-ray taken. The splints are reapplied and fixed in such a way that movements of the distal part of the limb—hand or foot—are permitted. Every day the splints are removed, the proximal and distal joints moved actively and passively in flexion and extension, but in the case of the forearm not in pronation and supination, owing to the lateral strain put upon the bones in this movement; the limb is exposed for half an hour a day to the heat and light of a

radiant heat lamp, and gentle massage of the limb is carried out and the splints reapplied. Under this treatment more rapid union and ossification of the graft have taken place, and fewer fractures have been recorded.

At the end of eight to twelve weeks all retentive apparatus is discarded, except in the case of weight-bearing parts of the body.

To sum up:—

1. All risk of sepsis should be avoided, and the presence of latent sepsis negatived by the application of radiant heat to the injured part.

2. All adherent scars of the skin in the vicinity of the seat of the proposed bone graft should be removed and healthy, mobile skin used to cover the operation area.

3. Whatever shape of graft is used, it should have comparatively long contact with the recipient bone at each end, and be closely and firmly fixed to the recipient bone.

4. The ideal form of fixation of the graft to the host bone is by absorbent sutures, but in certain cases metal screws, pins, or plates are of value to obtain the best and speediest results.

5. Early passive and active movements, massage, radiant heat, etc., should be made use of to encourage osteogenesis and prevent fracture of the graft.

Discussion.

Sir David Wallace congratulated Mr Morison on the excellent paper he had so lucidly presented to the Society, and referred in particular to the value of the X-ray photographs, which showed the results of his operations. He pointed out that as a result of the improvement in this type of surgical work during and since the war, many men had been enabled to undertake work which otherwise would have been impossible. He was interested in Mr Morison's method of determining, before operation, whether the risk of sepsis was present or not, and referred to the help which radiant heat might give in other spheres of surgery.

Mr Scot Skirving emphasised the necessity of having the bone graft as deeply placed as possible and really well covered by soft parts. This was easy to do in the upper arm, but difficult and sometimes impossible in the case of the tibia. He suggested that the large, thick pedicle grafts of the soft parts Mr Morison had referred to ought to be very helpful. Another cause of failure in hospital was sending the patients out too soon. He asked if Mr Morison had had experience of civil cases, such as filling up gaps after excision of bones for acute osteomyelitis and, if so, if these cases differed in

any way from the war cases, and was the latent sepsis less. Finally he asked if the employment of a heterogeneous graft—say ox bone—was a thing of the past.

Mr Mercer said it was interesting to compare the methods that had been described with those that are in use in Edinburgh. For the discovery of latent sepsis we achieved probably the same results by a different method, a hot soak being applied to the scar for five to ten minutes, to cause an œdema, such as is described by the German surgeons in the physio-therapeutic treatment of congenital wryneck. This was followed by heavy deep massage, and he had never seen a case so treated that did not fail to respond if there was latent sepsis in the scar tissue. After using most methods of fixation for the graft, he had come to the conclusion that the most satisfactory was either brass or silver wire. He did not put wire round the graft but fixed it longitudinally, two holes being fixed at either end of the graft and two each in the two fragments of the parent bone; no encircling, therefore, took place and when twisted up tightly one was able to move all the joints of the affected limb and yet get no movement at the graft, there being complete rigidity. This firm rigidity made a perfect result much more certain. The plaster cast was kept on for a much longer period than Mr Morison found necessary. He thought it was essential to protect the graft, particularly from the eighth to twelfth week as this time it was at its weakest, absorption having taken place to a great extent, and the laying down of new bone not yet having proceeded to any great extent. He was sorry that Mr Morison had not been able to show more end results, but he would like to ask him if he could tell what his percentage of failures was in his series of cases.

He pointed out that there seemed to be a great diversity of opinion in regard to this, as a recent writer recorded three failures in seventy-seven, while the Mayo Clinic and Williams both had about 20 per cent. of failures.

Mr J. J. M. Shaw expressed agreement with Mr Morison in regard to the advantages of carefully controlled movement at an early date as a means of preserving the full function of the related joints and hastening the consolidation of the graft. In fractures of the mandible with bony loss, a block of bone could always be obtained from the iliac crest of sufficient size to permit of careful fashioning and the apposition of a large area of graft to recipient bone. In these cases it had become the practice to shorten the period of complete immobilisation in double cap splints to two or three weeks.

With reference to the preliminary removal of scar and the provision of a sound covering for the graft, the tube pedicle which carried a certain thickness of subcutaneous fat in addition to skin was of great service and yielded in the new situation the protection which most closely resembled that of the original tissues.

THE OCCUPATION-CURE IN NEURASTHENIA.*

By A. J. BROCK, M.D.

THOUGH this short paper must necessarily consist for the most part of generalisations, I wish to state that these generalisations are entirely based upon personal experience with patients; they are an attempt to rationalise what experience has taught me. Moreover, I cannot produce cases for you to see; the procedure here advocated is one of re-education, and it is impossible to re-educate a patient in a few minutes on a public platform.

The psychogenic causation—that is, the essentially mental origin—of most of the psychoneuroses does not seem to me nowadays to need any demonstration. Previous to our day it was generally assumed that "a physical basis" would eventually be found for all mental disorders; psychotherapeutic methods were assumed to be at the best mere makeshifts. Undoubtedly everybody would nowadays agree that all mental processes, whether healthy or morbid, must be accompanied by changes of a chemical and physical nature in the nervous tissue. Experience has shown us, however, that from a practical point of view—that is, if we want to cure our patients—we do better to approach the majority of these conditions primarily from the mental aspect. In fact we probably often do this even when we do not know we are doing it. In view of recent experience, especially since 1914, it becomes more than ever probable that many of the elaborate physical methods which used to be employed in the treatment of neurasthenia owed much, if not most, or all, of their efficacy (where they were efficacious) to mental rather than to physiological principles. From such generalisations one obviously excepts cases directly dependent on gross organic lesions, extreme toxæmia, or the like.

Why do I say that the psychogenic origin of most of the psychoneuroses hardly needs any demonstration at the present day? Surely in ordinary life our way of dealing with a foolish or unreasonable person is by what may be called mental or moral methods. We attempt by sympathetic handling to arrive, in the first place, at his point of view. We then discuss the matter with him, and try by argument and persuasion to bring him to a sounder way of thinking. This is surely nothing less than psychotherapy in a small way. The difference between

* Read 17th January 1923.

the mere foolishness and crotchetiness of everyday life and the obsessions and phobias of neurasthenia, or even the delusions of insanity, appears to me rather a matter of degree than of kind. Indeed hard-and-fast categories would seem to be less relevant in practical psychology than in any other science.

Not only in their pathology, then, but in their treatment also, these conditions are not divided. When treatment is still possible, that of the severer degrees will be no less psychotherapeutic in nature than that for the minor degrees.

History will probably recognise Sigmund Freud to have been the chief representative at the beginning of the twentieth century of this renewed insistence upon the psychogenic factor in mental pathology. Thus his position will in various ways correspond to that of, say, Franz Joseph Gall during the time of social and political upheaval of a hundred years ago.

Gall like Freud took his stand upon subconscious factors—what he called "propensities." From the practical standpoint, it is true that he attached undue importance to localisation of these propensities in the cerebral cortex. Furthermore, his followers for the most part played havoc with his teaching by attempting to erect it into a rigid system—to introduce, in fact, just these hard-and-fast lines which we so particularly deprecate in psychology. Auguste Comte says that most of Gall's followers "as is too often the case, resembled him in nothing but his errors." Hence the excesses and the excessive claims of what came to be called Phrenology. Nevertheless we must not blame the master for the faults of his disciples; Gall's own position is secure. Should a proof be needed of the remarkable acceptance which his views m with from many of the most prominent representatives medicine at that time, it may be conveniently found recent work by Dr Bernard Hollander of London (*In of the Soul*), to which I would refer anyone who is in ed in pursuing this parallel further.

In Edinburgh at that period the psychologica s of Gall were espoused with particular enthusiasm, a will remember, by Dr Andrew Combe and by his br George Combe, the latter a justly renowned educationist or of *The Constitution of Man* (1828), and founder of the Trust.

In passing, it is of interest to note that like Freud, was an alumnus of the Vienna School.

Now, besides being the typical representative of this modern reawakening of interest in psychology, Freud's peculiar glory has been to bring prominently before us the idea of the Subconscious—that is of a powerful activity constantly working below, or at the back of, the conscious mind. In this connection, and taking, as it seems to me, his stand mainly on pathology, Freud has laid stress on the importance of sexual preoccupations, and even obsessions, as factors in moulding people's thoughts.

Quite recently, again, M. Coué has been demonstrating another prevalent symptom which also appears to be in the main pathological, namely the remarkable suggestibility, one might even say gullibility, of the average individual, particularly when he acts, as he tends increasingly to do, in crowds. I take this to be the factor to which Professor Edwin Bramwell in a recent interesting address referred as "Credulity," and whose retarding influence on the progress of medical science in general he strongly emphasised.

It is certainly a pity that so many people are in our day obsessed with the merely physical and egotistical side of sex, but undoubtedly increasing numbers are, and it is good that Freud and his followers should have reminded us of this fact. Then, to touch on Coué's demonstration: it is a pity that so many people should be suffering from over-hypnotisability—that they should be so much the victims of their imaginations, of any passing idea. M. Coué, however, has done an undoubted service by demonstrating afresh the prevalence of this state of affairs among us.

Now, as regards treatment: Freud has supplied us with an elaborate and effective method of extracting foreign bodies (the so-called complexes), which often become lodged in the subconscious depths of the mind and which are inaccessible to the psychotherapeutic methods of everyday practice. Coué, again, has more generally reminded us of the extreme value of thought-control and of mental self-discipline in combating gullibility. This gospel has of course been preached frequently by many medical men, notably, for example, in recent times by the late Dr Paul Dubois of Berne.

Now Coué's method, though valuable in many cases, is undoubtedly too blind to the complexity of causation—in a word, too superficial—to be justified in claiming the status of a complete system of psychotherapy. And to do him justice, M. Coué, I fancy, would hardly advance such a claim. He merely says, I think, "This helps."

In relation to the problem of Freudian psychoanalysis, this may be said: Over and above the cases that are cured when their particular phobia is removed or conflict resolved, there is a considerable class of cases in which the particular phobia or worry seems to constitute rather a symptom than the essence of the illness. In such cases, when the special obsession has been removed the patient remains well for a while—and then relapses. His trouble has been less a particular conflict or fear or worry than a general fearfulness, a general tendency to worry.

Now, it is for this class of case—and it is by no means a small class—that it seems to me re-education is particularly required, and here again we must go beyond the specifically Freudian no less than the specifically Couéan. The principle is to advance from analysis to synthesis; having disentangled the knots of our wool, the next step is to weave it into a pattern.

What seems to me to be at bottom mainly wrong in the type of cases referred to is that they are afraid of acting. Their phobias are not so much a dread of things as a dread of acting upon things—a dread, as we say, of facing the music. Man is at bottom not so much a being, an existence, as an activity; he is essentially "geared for action." This I take to be the philosophy of such recent authorities as William James, Henri Bergson, or Rudolph Eucken, and I confess that my experience, such as it has been, leads me to agree with them. A large part of present-day neurasthenia would seem to come from the fact that people are more and more failing to express themselves. We are all so wedged in that even our opportunities of acting for ourselves are limited. This is largely the censorship of circumstances (the *Zensur*) with which Freud has familiarised us. To express ourselves more fully, therefore, and so to become less neurasthenic, we have to act.

But we cannot merely beat the air. As already said, we have to act upon something. Upon what have we to act?

One would be wrong in saying that recent psychotherapeutic theory has concerned itself with man merely as a being; it has certainly envisaged him as a historical being, as a process in time—that is, as a patient with a history, an anamnesis. But I think that more stress yet will have to be laid on the reaction between this historic being and its environment, and particularly in a prognostic sense—in relation to the future.

The Occupation-Cure in Neurasthenia

We must consider the psyche as a patient *with a job ahead of it.* History must, if I may so say, be supplemented by geography. We must consider the psyche's environment, and that not only in the past but in the future.

The simple fact is that organisms without environments do not exist. The reality of life is a relationship, a dynamic relation and constant interaction between organism and environment. Therefore, while the organism may be abstracted for the purpose of theory, we must never forget that this is but an abstraction, and that in treatment we are bound to recognise the whole fact and to fit the organism into its milieu.

To what kind of environment, then, is the human organism, the psyche, by its nature related? To a social environment. Aristotle has said Man is a *politikon zoön* (πολιτικον ζῷον) a social animal. Aristotle meant by this that man can only develop and express his full human nature within society—just, say, as a hive-bee is nothing, and in a sense has no significance, when abstracted from the hive. But *politikon zoön* means more than a mere *social* animal; *politikon* means pertaining to a polis (πολις)—it means *civic.* Aristotle says in effect that it is only as an inhabitant of a definite concrete city-state that man can express himself; it is necessary for the fullest development of one's powers that one should be in active personal daily relationship with one's fellow-citizens. This was possible in the old Greek city-states, which were small—not bigger, for example, than our Greater Edinburgh. Observe that it becomes increasingly difficult under modern conditions, and, even where conditions make it relatively possible, it is no longer cherished as an ideal. For personal intercourse we more and more substitute the purely official or business relationship between man and man. Machinery is replacing the human touch—and not merely the literal machinery of telephones, typewriters, and the like, but administrative machinery also.

Let us apply these principles, then, to our common type of neurasthenic, who may be said at bottom to be suffering from *ergophobia*—from a dread of exerting himself. Note that he may have good reasons for this dread. His heredity may be bad. His education may have been neglected; he may never have been taught to exert himself. Further, his present circumstances may be very difficult; at the moment many

of our patients are faced with all sorts of environmental difficulties—economic, domestic, and so forth, and all these interacting with one another. Many people are still suffering from war-strain, and the Frightfulness of war was a very real thing. We must have the greatest patience with these sufferers. Owing to the complexity of circumstances, the temptation to deal with them piecemeal (to take, as the saying is, "one thing at a time"—that is, to take the disease symptom by symptom) is often nearly irresistible. Nevertheless, a clue must be found for treating these circumstances as a whole.

Quite a lot of our patients, even with circumstances eminently suitable for them, are yet refusing to exert themselves; they are not utilising their circumstances. Hence their self-respect, their self-confidence—their "faith," in short—declines more and more, and, if they continue living at all, it is only by increasing resort to various kinds of dopes. Many of our more well-to-do patients, rather than exert themselves in the slightest way, will bid adieu to their responsibilities (letting others undertake these) and either flee the country or indulge in a quasi-hysterical "nervous breakdown," the very name of which invariably draws to them that sympathy for which they so passionately crave. A nervous breakdown is of course sometimes excusable—but not by any means always.

This prevalent underlying debility may be obviously called by many names. From one very practical point of view it may be looked on as an *aboulia*—that is, as a weakness of the will. I am aware that determinists deny the existence of will, and will is certainly not to be discerned either by the senses or by the reason reflecting upon what the senses disclose. Further, it is more or less absent in the insane. Nevertheless, this inexplicable will is appreciated as a fact in the ordinary everyday experience of any healthy individual. We appreciate that will exists—when we use it.

Let me quote from a leading article which appeared in the *Lancet* in the year 1909. "It is, we venture to think, *one of the most extraordinary paradoxes of our time* that though the modern school of psychology is . . . usually materialistic in its teaching, insisting that will, attention, and conative processes are results not causes, and that there are no such things as primitive faculties in the direction of compelling forces, yet that the latest remedial measures put forward as of extreme validity involve an appeal to that very will and attention whose existence in the laboratory is strenuously denied. Monistic materialism

may be our creed, but if so, it is *a creed which we disregard in practice.*" (*Lancet*, 13th October 1909. Italics mine.)

If a metaphysical explanation of man's freedom in modern philosophical terms be required, no better authority probably can be found than Bergson. But it must be again and again emphasised that a proof of the existence of freewill is in the hands of the least intellectually gifted among us; the fact is, it can be apprehended directly by the man-in-the-street in his everyday experience.

The Freudian theory of the psyche seems to me to be more particularly applicable to pathological conditions (and we have seen how widespread these pathological conditions are), while the Bergsonian psychology is more adapted to explain healthy minds, possessed of normal self-control. On this view psychotherapy may be looked on as the process of bringing the mind from a Freudian to a Bergsonian condition.

It is noteworthy that the chief popular educating agency of the people, viz., the daily press, constantly belittles the idea that man can help himself. Thus it flaunts before its readers all cases in which man is carried away by his passions and weaknesses, and scarcely so much as refers to the normal life of humanity, the daily heroism of the home, the field, and the workshop. As has been wittily said, the press is more concerned with one individual who throws his chair out of the window than with fifty who use that article of furniture in the ordinary way.

To take a small but very actual and significant example of this tendency from the papers at hand: I observed a fortnight ago, at New Year time, that practically all the papers which have a comic column distinguished themselves by a joke about the making of New Year resolutions. They all indicated in effect that it is futile to make such resolutions—that we cannot keep them.

Observe that the public enjoy such literature—mainly, of course, because it makes no demand on them. It says, in effect, Don't try to help yourselves; the thing can't be done. And further, We will do your thinking for you.

You will observe that this popular outlook and propaganda with regard to the will is but the counterpart of an advancing school of academic psychology which holds (for example, in criminology) that man is not responsible for his actions. The fact, of course, is that the average criminal is *less* responsible for his actions than an ordinary man, less able to control himself.

But we must not generalise for humanity from observations on the criminal.

Now, it is aboulia, the weakness of this will, which it behoves the doctor to remove in his patient. Whether the condition be mainly of exogenous or endogenous origin, the patient must be encouraged to action, invited to work. Thus his will will be strengthened.

Now, it is in getting such people to work that the doctor's main difficulty lies. Patients of this type are in a sense malingerers—but, I believe, in far the most instances sub-conscious malingerers, such as we so often met with during the war. These people will say, I can't work. This is practically never true. The truth is that they find it *very difficult* to work, and the difference in these two outlooks, as also the value of strengthening their wills by a daily forcing of themselves to action, must be patiently and persistently laid before their conscious minds by the doctor, until it sinks into their subconscious minds and begins to take root there, so to speak, and to germinate.

But of course there are two kinds of work: firstly, that imposed from without, by what may be called the drill-sergeant method—the work done, for example, by a gang of prisoners or by a labour squad; and secondly, there is congenial self-expressive work—that which an individual feels joy in doing; this is inspired from within; it is spontaneous, artistic, creative.

The work prescribed should, in the first place, be congenial; it should be work for which the patient has a natural aptitude, and, if the patient be grown-up, then work of which he has had some experience.

In this work—if once we can persuade him to conquer himself, to use his own will—he will find the *means* of expressing himself creatively—that is, with real inspiration, as an artist does.

But even professional artists, it is observed, may suffer from neurasthenia, and I think this is largely because in so many cases their work is but "Art for Art's sake"; it is too purely organismal, if I may so say, and is too unrelated to the artist's social environment. Man, let it be repeated, is a social—more exactly a civic—animal. Our neurasthenic patients need to be socialised. They are commonly very unsociable, irritable, "up against" everybody. They must force themselves to get over this, and the doctor must not force them but help them to force themselves.

The artist should try to see his self-expressive work as part of the general work of the community he lives in. He will better do this the better he knows the place he lives in, and for this reason I encourage my patients whenever possible to study for themselves the origin and growth of the social milieu that they inhabit—as, for example, when they live in Edinburgh, then Edinburgh. I believe that in order to be fully alive one must know the world, and that the first condition for knowing the world is to know that part of the world in which one lives. I do not mean so much the political unit in which one votes or pays taxes, as the actual part of the world in which one spends one's daily life and does one's daily work. Similarly, one cannot understand humanity without coming into contact with actual human beings; it is desirable wherever possible to re-educate the patient in relation to his own domestic and ordinary social circle; we desire to fit him eventually to live in these without artificial support, and the best way to learn to swim is to go into the water.

Nevertheless, as we know, there are many cases which for various reasons must be removed temporarily from their ordinary environment. That period should be the minimum possible, if our aim is to make our patient an efficient citizen. Certain cases, of course, have to be withdrawn permanently from the stresses of everyday life, but I am considering here only cases which are curable.

The treatment of each special case of neurasthenia is such a highly individual matter that any attempt to give examples is almost certain to throw the whole picture out of focus.

Above all each of our patients must get to work and *produce something*. This must be something that he feels he can put his personality into, and it must also appeal to him as being *of use*. The more it is related to the life about him, the more will its usefulness be clear to him.

Under more natural conditions (as in remote self-supporting village-communities) the individual sees his world as a whole, and his mental serenity comes largely from his seeing this—as also from seeing the relation of his special work to this whole; he sees the product of his labour locally consumed or utilised. The complexity of life is, generally speaking, less in country places, and it is often desirable to remove our patients from town to country. In the country one has not only healthful physical conditions, but not too many alluring distractions, and when one works one tends to see more clearly the result of one's

labour. Many of our depressed patients, however, find sudden removal to the country too trying, and it may have to be done gradually, and in any case should never be done unless the patient has some natural liking for country life, as well as an aptitude and experience in regard to it.

The treatment of neurasthenics of the wage-earning class presents an especial difficulty. They have usually little or no choice of occupation, and what occupation they have is usually of a dull, mechanical, and routine nature. If a cure can be applied to those people at all it must be in their short leisure hours; their work gives them little scope for feeling the joy of artistic creation. The treatment of the neurasthenic labouring man must, to a large extent, be left to nature, symptoms being treated as they arise. If he is quite unable to compete in the labour market, he should, if possible, be sent with his family to some quiet place where competition is less keen, and there provided with simple occupation, and perhaps given meantime some State aid. The fact that there are vast numbers of men unemployed in the country just now is from the psychological point of view profoundly disquieting. If my contention as to the result of idleness be in any way correct—and I have not spoken of it as complicated by such factors as poverty, wretchedness, and semi-starvation — then there must be developing amongst large sections of our British population a psychological condition which, if it cannot be appeased at least temporarily by some kind of dopes, is almost bound to find outlet in widespread violence and destructiveness. Men lose their faith if they are not working, and a man who has lost his faith easily loses his head.

Education.

I have suggested that our neurasthenic patient should, where possible, be got to apply his mind to the study of his own district. If this proposal be thought too far-fetched, let me point out that the principle is at least recognised in educational theory; why not, then, also in re-educational? Further, education and medicine nowadays are more and more becoming one. In view of recent psychological discovery, it is surely clear that the more one becomes a doctor the more one becomes a psychotherapist, and that the more one becomes a psychotherapist the more one becomes a re-educator. But prevention is better than cure, and hence we doctors must try to see the problem of education and re-education as one.

Education in fact is obviously the main constituent of what may be called Preventive Mental Medicine. And hence comes the pressing need for us to take counsel with our educational friends and to institute a growing collaboration with them. In view of the recent breakdown, moral and mental, which we doctors have been called upon to cope with, we are, I think, in a position to point out to educationists what have been some of the main errors in pre-war education. Briefly I would suggest two. Firstly, the child's education has not borne enough reference to his environment; this has directly unfitted him for facing actual circumstances when urgently called upon to do so in later life—it has bred a predisposition for organism to become dissociated from circumstances.

Secondly, pre-war educational theory by presenting knowledge as a series of disconnected "subjects," has directly predisposed to that dissociation or fragmentation of the mind which is a leading characteristic of the typical psychoneurosis.

As education improves, there will be increasingly fewer cases of nervous instability and nervous breakdown for the doctors to treat.

Now, one of the most promising methods at present under discussion in the educational world is what is called Regional Survey. The principle is that, since the child has to get to know the world and its history, it will best begin by getting to know that part of the world in which it lives, that part with which it is in actual daily contact. The various "subjects" which the school-books write learnedly about have to be sought first in the student's immediate neighbourhood. There they will be found not only concretely represented, but also, what is equally important, in their mutual relationships.

This principle appears to give a feeling of reality and an interest to the child's studies unobtainable in any other way. It gives the child the preliminary mental balance which will be the best guarantee for stability in later life. More exactly, education does not *give* the child this—it only continues and widens the instinctive knowledge the child has inherited, its natural interest in practical and concrete life, its profound sense of proportion and of humour. Upon this foundation education implants intellectual learning.

Speaking, then, from the point of view of psychological prophylaxis, I beg to submit that the best foundation for the education of Edinburgh children in the future will be a know-

ledge of the community they live in—considered both in time and space. To this central point of interest all their special studies should be as far as possible subordinated. There is already a so-called Regional Survey Association in existence, with its headquarters in London, and with several branches throughout Great Britain, and to this I would respectfully draw the attention of any of my medical brethren who do not know of it.

To sum up: a large number of our cases are suffering from aboulia or ergophobia—their wills are weak, they are work-shy. For this they need ergotherapy. The work given should be congenial. It will only be congenial in so far as it is expressive, firstly, of the patient's unique personality, and secondly, in so far as it bears reference to the essential nature of his milieu. This milieu is social; therefore the doctor must consider this also and become a sociologist as well as a psychologist. This milieu is a unity, and it is fundamentally important that the patient should deal with it as a unity and not piecemeal; if he be a specialist he must subordinate his specialism to the general view.

Finally, as prevention is better than cure, the medical psychologist must more and more interest himself in education. Co-operation between the doctor and schoolmaster is already overdue, and should be proceeded with at once.

Discussion.

Dr Garden Blaikie pointed out that lack of sound teaching on the basal facts of life gave children a wrong attitude towards sex questions from the beginning. She suggested that the school curriculum should include nature-study, by which children would become familiar with the great processes of growth and reproduction. Later some simple teaching might be given on the structure and function of the human body—a mere outline of anatomy and physiology. She believed that frank, wholesome teaching, wisely given, would do much to prevent unhealthy thinking and acting later in life.

Dr W. T. Ritchie although he concurred with Dr Brock as to the beneficial effects of psychotherapy in selected cases, considered that there was an organic basis in a very considerable proportion of "functional" cases, and that the necessity for treating the underlying organic disease should never be lost sight of. He instanced a number of war "neurasthenics" who were found to give a positive Wassermann reaction.

Dr John Stevens said that he feared that psychotherapists were sometimes apt to overlook the physical basis of life, to regard human beings as having reached the stage of disembodied spirits, and consequently to attribute to purely mental or psychical processes symptoms really associated with physical changes in the organism, which from their nature or minuteness might be difficult or impossible of detection. He said that a condition of social or political neurasthenia had attacked the mass of the population through the increasing tendency to look to the State to do for the people more and more of what they ought to do for themselves, thereby seriously impairing individual initiative and responsibility. This, he pointed out, is well exemplified by the recent invasions of the State into the sphere of Medicine, involving a grave and increasing menace to the free and independent practice of that profession, and a lowering of the status of the great mass of people swept into the net of State Medical Socialism. As an example of the error of attributing symptoms to psychical or functional conditions without first excluding ascertainable physical causes, he instanced a case of neurasthenia in which the left side of the body was specially affected, one of the symptoms being deafness of the left ear. The patient had been encouraged to expect the hearing to return with the recovery from the neurasthenia. An examination of the left ear, however, revealed the fact that the meatus was blocked with wax, the removal of which restored to him normal hearing without having to wait for recovery from the neurasthenia.

Dr Walker, referring to Dr Stevens' remarks, said that it was not psychotherapists who treated patients as disembodied spirits. She thought they treated them more as human beings than any other class of physicians. She pointed out that it was a primary error in our educational system to treat children as disembodied spirits, and to train them without sufficient relation to their environment. This tendency, she said, was continued later in school life, *e.g.*, where all manner of subjects find place in a curriculum which ignores elementary physiology and anatomy. Such dissociations from surroundings, she thought, rendered it more difficult for the individual to maintain balance when called on to meet some sudden stress in everyday life.

Dr Brock in reply said: With regard to the point raised by Dr Garden Blaikie and Dr Walker, I think that instruction in the physiology of human reproduction would have to be given, if given at all, with the extremest circumspection, otherwise it would tend to convey the idea that love and marriage were in essence nothing more than a physiological matter. I approve of some instruction in anatomy and physiology being given; I would lay more stress, however, on the child gaining an acquaintance with its immediate environment in the ordinary sense than with its somatic environment.

I think lay people who read medical books often think far too much about their insides—in fact, become neurasthenic on the subject.

I agree with Dr Ritchie that cases are often carelessly labelled functional. As regards the Wassermann cases, however, I would wish proof that their nervous symptoms were entirely due to the syphilitic toxin; the knowledge, for example, that one has or may have syphilis is a very worrying one; the term "syphilophobia" proves this.

Dr Stevens advocates moral methods for dealing with lack of self-reliance, and my proposal is merely an extension of such methods to allied, but more definitely pathological conditions. I agree that such conditions have a physiological aspect, but do not consider that of primary importance in treatment.

In conclusion, I would emphasise once more the necessity for doctors interesting themselves in education, this being the chief field of prophylaxis against neurasthenia and even more serious mental disorders.

The President moved the thanks of the Meeting to Dr Brock for his interesting paper.

Meeting—17th January 1923.

EXHIBITION OF PATIENTS.

(1) *Mr Wilkie* showed a case of **Pseudo-Coxalgia of the Right Hip Joint** in a boy of 18 years. He was shown to the Society in 1913 and again in 1919. During the ten years which have elapsed since the disease was first recognised, no treatment had been carried out and at no time had the boy been laid up, even for a day. The disease has now reached the quiescent stage, the boy being quite free of all pain, although having a definite but not pronounced limp. X-ray photographs taken in 1913, 1918, 1919, and 1923 showed the progressive changes of the disease. The question of etiology was raised and the opinion expressed that a mild subacute infective process was probably the underlying cause of the condition.

(2) *Dr Fergus Hewat* showed a case of **Mediastinal Tumour.**—A. S., aged 49. *History*—Fit until influenza in February 1922. In bed one week. Noticed weakness of lower limbs in May 1922. Kept at work till November, becoming gradually weaker. Pains in chest and irritable cough began three months before admission to hospital. He has lost nearly 2 st. in weight, but picked up 8 lb. in five weeks in hospital. *Physical examination*—Impaired percussion note on left side of chest both front and back. Auscultation shows feeble breath sounds of vesicular quality throughout with friction in infra-axillary region. X-ray of chest showed well-defined shadow extending above and to the left of the heart. Wassermann of blood

negative. Blood count showed mild secondary anæmia. The tumour is probably a lympho-sarcoma.

(3) *Dr Goodall* showed a boy suffering from **Progressive Muscular Atrophy**, not of the usual juvenile type. The muscles most affected were the deltoids, rhomboids, infraspinatus, and triceps. All of these showed reaction of degeneration. The condition had been slowly progressive for four years. The affected muscles showed fibrillar tremors and the knee jerks were increased.

(4) *Dr W. T. Ritchie* showed a case of **Facio-scapulo-humeral Myopathy** in a female patient, aged 32, in whom atrophy of facial muscles began at the age of 16. The facial atrophy is mainly left-sided. The trapezius, serratus magnus, pectoralis major, latissimus dorsi, rhomboids, biceps, and triceps on both sides are atrophied. The shoulder girdles present a characteristic deformity, falling downwards and forwards. There is lordosis, a waddling gait, atrophy of the extensors of the ankle joints; pseudo-hypertrophy of the lips, deltoids, infraspinati, and glutei. There is no fibrillar tremor; the electrical excitability of the atrophied muscles shows a simple quantitative diminution without reaction of degeneration. The only relation similarly affected was the patient's mother.

Meeting—7th March 1923.

EXHIBITION OF PATIENTS.

Dr H. Whitridge Davies described a case of **tetany following thyroidectomy.** The patient, an unmarried woman, aged 22, was admitted to the Royal Infirmary under the care of Professor Meakins in February 1921. She gave a typical history and clinical signs of Graves' disease, and was transferred to Sir Harold Stiles, who performed partial thyroidectomy of the left lateral lobe. This operation did not appear to give much relief, but the patient went home and was re-admitted to the Royal Infirmary in January 1923. At this time her symptoms were present in a marked degree, and a further operation was decided upon. This consisted in resection of the right lobe of the thyroid gland. Six days after operation she complained of stiffness of legs and arms, and was observed to have the characteristic attitude of tetany. Trousseau's and Chvostek's signs were present to a marked degree. She was given parathyroid extract, gr. 1/10, night and morning, and for a few days this seemed to control the spasms, but after a few more days the symptoms became much worse. The parathyroid extract was continued, but she was given in addition a dram of calcium lactate every two hours. This again relieved the symptoms for several days, although Chvostek's and Trousseau's signs remained positive. After these few days of relief the tetany again became much worse,

and was associated with frequent and distressing attacks of laryngismus stridulus. These symptoms were relieved only when the parathyroid extract was administered subcutaneously. Up to the time of writing (three weeks later) the symptoms have been greatly improved. Chvostek's sign gradually became less marked until it completely disappeared, although Trousseau's sign remained present. Attempts were made to reduce the dosage of calcium lactate and of parathyroid extract, but resulted in a partial return of symptoms.

The patient showed definite evidence of alkalosis, using this term in the sense of an increased carbon dioxide combining power of the blood. It was not possible to estimate guanidine or methyl-guanidine in the blood and urine, but indirect evidence of abnormal amounts of these substances was given by a high non-protein nitrogen as well as a high creatinine content of the blood (the latter was determined by Folin's method). Sections cut (by Mr J. N. J. Hartley) of the excised thyroid showed no signs of any parathyroid tissue. The clinical lesson to be learned from this case is that parathyroid extract given by mouth appeared to be quite without effect. Neither parathyroid extract subcutaneously nor calcium lactate when given alone had any permanent effect, but when given together marked improvement occurred.

A more complete account of clinical and biochemical investigations of this case, together with a critical review of the subject, will be published at a later date.

Dr Goodall showed a patient to illustrate **the effect of non-specific protein therapy**. This was a miner, aged 34, who had suffered from chronic rheumatoid arthritis for nine years. He had been unable to work for three years. His teeth had been removed and he had received various forms of treatment, including a course of injections of an autogenous vaccine made from his gums. There had been little benefit. Latterly the man could only crawl on his hands and knees when he first got up in the morning, but later in the day he could walk with the aid of two sticks. He had not been able to touch his chin for over a year. Radiograms showed typical changes in his shoulders, elbows, wrists, knees, and ankles. After a preliminary desensitising dose, he received 0.2 grm. of peptone by intramuscular injection. The next day his temperature reached 103° F., and the slightest movement of the affected joints was attended with severe pain. When this subsided there was an immense improvement. A second injection of 0.3 grm. was given a week later, and again this was followed by a day of misery. When the patient was shown three weeks after the second injection, he was able to walk briskly and could extend his arms at full length above his head. The movements of all his joints were free and painless.

Sir David Wallace showed—(1) a case of **exophthalmic goitre.** Mrs U., aged 52. First noticed swelling October 1920, at which date exophthalmos present. Treated medically for a year; tachycardia gradually increased. Lost two stones in weight, and became very weak.

Operation (18th February 1921). Uninterrupted recovery. Able for housework, and regained weight. Recently noticed swelling at left side of neck, but no toxic symptoms manifested.

(2) A case of **epithelioma of tongue.** R. H., aged 41. Noticed ulcer two months ago. Now much induration at base of ulcer. No palpable glands in neck.

Operation (9th November 1921). Right submaxillary region cleared out. Mandible divided in middle line, and half of tongue with floor of mouth removed. Uninterrupted recovery.

Microscopic examination: Ulcer, a squamous epithelioma. Largest gland removed shows no sign of metastasis. At present no sign of recurrence.

Dr J. V. Paterson showed a case of **spontaneous arteriovenous aneurism of the carotid artery** in the cavernous sinus, causing pulsating exophthalmos and paralysis of the sixth nerve.

The patient, a married woman, aged 34, of rather slight build but healthy appearance, living in the country, came to the Eye Department on 27th February 1923, complaining of double vision. Patient had been twice married and was the mother of six healthy children. The last baby was born about six weeks before her visit to the Infirmary. The history given by the patient was that when she was milking a cow about four months ago, she was seized with a violent pain over the vertex on the right side. She did not feel sick or faint, but went on with her work. A dull headache remained, and about two weeks later she began to notice a peculiar rushing noise in her head. The headache appears to have ceased to trouble her. No history of any severe injury or fall could be obtained. The double vision began about three weeks ago, and it was this that led her to seek advice.

On examination the vision was found to be quite good in each eye, the fundi normal with perhaps a slight dilatation of the retinal veins on the right side. Examination also showed obvious internal squint of the right eye, and complete inability to move the eye to the right. The upper eyelid was slightly œdematous with dilated veins showing. The veins of the conjunctiva were also somewhat dilated. Proptosis of the right eye was present, but only to a very slight extent. When the eye was pressed back into the orbit, distinct pulsation could be felt. The veins at the angle of the orbit and the root of the nose were distinctly dilated, and pulsation was very obvious on pressure with the finger. A fine thrill could also be felt. Auscultation

revealed the presence of a fairly loud soft systolic bruit, which was heard all over the head, but most marked on the right side and extending down the right side of the neck. Deep strong pressure over the carotid on the right side caused cessation of the bruit and the pulsation. The heart sounds were normal, the pulse 86, and the blood-pressure 130. A Wassermann reaction was taken but the result was not yet known.

Dr Paterson spoke of the extreme rarity of the formation of a spontaneous aneurism in this situation, while, as is well known, the traumatic variety is not uncommon after severe head injury or deep punctured wounds of the orbit. It was interesting to note that in many of these spontaneous cases there was a history of repeated pregnancy, and in some of the cases the symptoms apparently began during or shortly after labour. Another group of spontaneous cases occurred in old people with degenerated vessels.

With regard to the question of treatment, no operation was proposed as the symptoms appeared to be in no way urgent.

Dr Paterson also exhibited for Dr Traquair a dissection of the cavernous sinus and the carotid artery, showing its course from the base of the skull to its termination. Attention was specially directed towards: 1. The difference in structure between the carotid artery inside the sinus and outside the skull. Within the sinus the vessel is ampullated and its wall is about half as thick as in the neck. 2. The position of the sixth nerve, crossing and in contact with the ascending part of the artery in the sinus.

DISCUSSION ON INSOMNIA.*

(Abstract of Paper introducing the Discussion.)

By A. R. CUSHNY.

THE cause of sleep is still a matter of discussion at the hands of physiologists and psychologists. Is it induced by the presence of waste products of the other tissues acting upon the nerve cells or by exhaustion of the nerve cells through their activity? Every now and then the thesis is brought forward that sleep is caused by some special product of activity—fifty years ago by the lactic acid of muscular exertion, more recently by some fatigue-toxin; but the great majority of the profession consider that the cause is the exhaustion of the cells by impulses from the periphery. Sleep is not so readily

* Held 7th February 1923.

induced by brain activity itself without muscular movement. Very often after prolonged mental exertion, sleep refuses to come, and this is true whether the mental activity is pleasant or unpleasant. On the other hand, sleep is much more likely to occur when mental activity leads to bodily exertion, and one of the circumstances that favours the oncoming of sleep is muscular exercise. It must not be too violent, for if the fatigue is excessive, sleep may be kept at bay by the discomfort of joints and muscles, perhaps even by impairment of the circulation.

This muscular activity is best taken in the open air, for in that case the reflex from the exposed skin, from the face mainly, comes into play. This much neglected face reflex, one of the most powerful therapeutic agencies, apparently arises from the maintenance of the coolness of the face, and is the main therapeutic factor in the out-of-door treatment of disease, in the open window habit, and the recovery of fainting, and other accidents, and is of great importance in inducing sleep.

Other agencies may be invoked—meals at late hours are to be avoided; dinner should be lighter than it often is; the bedroom should be well ventilated; bedclothes should not be heavier than is necessary; the feet should be kept warm. All these measures which are sometimes spoken of contemptuously as nursing treatment, are of great importance in the treatment of ordinary insomnia.

The course of sleep varies in its character in different people. The happiest are those to whom deep sleep comes rapidly, the stage of unconsciousness being greatest in half an hour to an hour after sleep begins; the sleep then becoming lighter until consciousness gradually returns in the morning. In others less fortunate, unconsciousness comes on gradually and fitfully, sometimes hours elapsing before the patient is really at rest; the sleep becomes slowly deeper until it reaches its maximum very late, often just before it has to be interrupted to begin the duties of a new day. In this form the patient never awakens with that sense of energy and well-being which is the characteristic result of healthful sleep, and in its worst form deep unconsciousness is not attained and the patient suffers from insomnia. This form of insomnia in the otherwise healthy is exceedingly difficult to treat. All the nursing measures should be taken to encourage it, out-door exercise with moderate exertion and the measures which have already been discussed.

Drugs should be avoided as long as possible. If a drug is used occasionally it should be one acting quickly and inducing deep sleep early.

The treatment of insomnia during illness is much simpler. Here the natural agencies promoting sleep cannot be applied, but on the other hand drugs are available, and it is of no serious concern if these act slowly and the brain be depressed for a longer time. In mental disease drugs may be used freely, and very often it is advisable to use those with a prolonged action.

Among the innumerable hypnotics available, the most important are chloral, paraldehyde, sulphonal, barbitone or veronal, and bromides. When sleeplessness arises from pain or muscular restlessness, this is of course treated with small doses of morphine or hyoscine.

Among the simple hypnotics, chloral is superior to the others. It is easy to take, acts quickly, and its effects pass off quickly. It has no significant action on the heart.

Paraldehyde is equally valuable, except that it has to be taken in large quantities. It has a disagreeable odour and taste, and this persists in the breath long after sleep has passed off.

Sulphonal is not suitable for insomnia in otherwise normal persons, because although it is easy to take, its effects are slow in coming on and last as long as twenty-four hours afterwards. While this is no drawback in illness, it hinders mental work in the morning hours.

The same is true of veronal, which is also slow-acting, although not so slow as sulphonal, but it is superior to sulphonal in the absence of poisoning effects upon the liver and blood.

Bromides are not very successful in cases of insomnia unless they are given continuously, and this involves a lessened mental activity in the day-time which is impossible for healthy people leading active lives.

Dr Ker said that he would approach the subject from a different standpoint from that of Professor Cushny, who had limited his remarks chiefly to insomnia in persons who were otherwise in good health. His own experience was, on the other hand, almost entirely restricted to febrile patients in urgent need of sleep. It would be generally agreed that in treating insomnia the most important thing was to ascertain the cause. Also that drugs should, whenever possible, be avoided, and, when given, prescribed for as short a time as possible. If it became necessary to continue their use it was a

good plan to ring the changes on several different hypnotic remedies so as to avoid either tolerance or the formation of a habit. As regards the causes of insomnia such common ones as discomfort in bed, too many or too few bedclothes, the height of the pillow, the ventilation of the room, cold feet, an empty stomach and so on, had to be remembered. Pain was, of course, a frequent cause. Certain conditions which modified the circulation of blood in the brain, such as sclerosis of the arteries from too much rigidity, or anæmia from want of tone of the vessels, might be found responsible. Lastly, the febrile state was very often of itself the cause of insomnia which was apt to be associated with headache and delirium.

As regards treatment, stress should be laid on simple measures, for the most part "nursing methods," to obtain sleep. Warmth to the feet, warmth to the stomach either by the external use of a fomentation or by the administration of hot drinks, whether of milk, beef-tea, or whisky toddy, were all useful. In the febrile state tepid or cold sponging was of value, partly no doubt because the temperature was slightly lowered and any tendency of the temperature to fall made it easier for the patient to fall asleep. A small dose of such a drug as phenacetin by relieving headache and slightly lowering the temperature was often effective.

If hypnotics had to be resorted to, so far as pain was concerned there was nothing like morphia and the opiates. As a student he had been taught that there were many limitations to the use of morphia, for instance in acute respiratory disease, in albuminuria and in young children. As he acquired experience he found it could very often be given with great advantage in such conditions. It was also invaluable for excited delirious patients who urgently required sleep. And was useful in cerebro-spinal meningitis, though it was well to remember to see that the spinal canal was well drained by lumbar puncture when it was employed as it appeared to increase the intracranial pressure.

For ordinary fever work, enteric or pneumonia cases, a combination of chloral hydrate and bromide of sodium worked very well. Bromidia was useful especially for children suffering from meningism or actual meningitis. Paraldehyde, the safest of all hypnotic drugs, was most effective when given in sufficient doses and repeated as required, and could be given by the rectum if preferred. It was an excellent remedy to use for insomnia either in adults or children suffering from scarlet fever, measles, or diphtheria. Sulphonal given four hours before sleep was desired, and followed up then by paraldehyde repeated if necessary, was one of his favourite drugs. He had not seen any ill effects follow its use, but he never gave it more than three nights running, using some other drug on the fourth night if necessary. It

had the advantage of keeping excited alcoholic patients asleep for the night, and rendering them comparatively quiet and tractable all next day.

Often combinations of drugs succeeded when one alone would fail. Good combinations were chloral and bromide sulphonal and paraldehyde, alcohol and opium as in a Dover's powder given with hot toddy. One drug appeared to put the patient in a condition to fall asleep and could be relied on to keep him asleep, the other was required to actually send him over.

No fever patients should be allowed to have two consecutive sleepless nights. When a drug is prescribed the nurse should always be told what to give if it does not act, and in some way sleep must be obtained. Otherwise the fever patient is left still sleepless, or perhaps even more wide awake, with an extra poison in his system, and no confidence in his doctor.

He had no real experience of suggestion beyond the giving of empty cachets and wafer papers and hypodermic injections of distilled water to patients who said they could not sleep without their usual treatment.

Professor George M. Robertson desired to associate himself with the expressions of appreciation uttered by the President and Dr Ker for the excellent opening address which Professor Cushny had delivered.

Professor Cushny began his address with an account of the physiology of sleep. He stated that there were two types of sleep. There was first the type in which the person, shortly after falling asleep—say in an hour or two—enjoyed the most profound sleep, and it was most difficult to waken him; the intensity of the sleep gradually became less and less so that he was easily wakened after six or seven hours. In the other form, according to Professor Cushny, the reverse process took place and sleep was light at the beginning and profound at the end so that it was difficult to waken the person in the morning. Professor Robertson was not aware of this second type of sleep. So far as his personal experience went, what happened was that the person tossed about during the early part of the night and did not go to sleep probably till about four or five in the morning. He then fell into a profound slumber, and consequently when the time came for wakening him, which was two or three hours after he had fallen asleep, he was enjoying the most profound period of physiological sleep.

Professor Robertson was interested in Professor Cushny's account of the effects of the face reflex. It was certain that a long day in a motor car had a distinct hypnotic influence. On the other hand there were many people who could not sleep when the wind was blowing on their faces and stimulating it. Such persons could only sleep

when they pulled the bedclothes over their heads, and when they inhaled an extra percentage of carbonic acid gas.

Professor Robertson thought there were two types of insomnia, which should be distinctly recognised by the physician, for the drugs necessary in their treatment required different properties. Of course he assumed that all natural means and favourable conditions would be employed before drugs were used. The one form of insomnia was that of the patient who could not go to sleep, who remained awake till the morning and only then slept. The other form of insomnia was that of the patient who slept at once on going to bed, and who wakened early in the morning and did not sleep again.

With regard to the treatment of the first variety, the best drug of all was paraldehyde, which was related to the alcohols, and which acted almost instantaneously. He had even seen patients sleep within a couple of minutes of getting it. It should not be administered to the patient till the patient was in bed and everything prepared for quiet sleep, so that its immediate action should take effect. Paraldehyde should always be given dissolved in 10 or 12 parts of water. It dissolved in 8 parts. It was an exceedingly safe drug and could be given in very large doses. The ordinary dose was 2 drams, but in cases of insomnia due to acute mental disease, it could be given in 3, 4, and 5 dram doses. It was better to give a big dose at once than to give two doses. He had known of more than a dozen patients who had taken 2 ounces of paraldehyde in one dose, and only one of these had died. This was a patient suffering from advanced phthisis in whose case elimination by the lungs was probably defective, and who was weak in any case. These patients were so perfectly unconscious that major operations could have been performed on them. He had also known of a patient taking regularly 8 ounces of paraldehyde every night—this case was a regular paraldehyde drunkard. The drawback to paraldehyde was the evanescent nature of its action. The patient tended to waken in the morning. Its action might be prolonged by the administration of bromide of potassium, administered before bedtime.

With regard to bromide, he believed its effects to be very much exaggerated. It was a poor hypnotic if administered alone. It no doubt had some action in allaying the excitability of the nervous system, but he placed very little faith in it.

Professor Robertson had been very interested to hear Professor Cushny's remarks regarding chloral. He was taught by Dr Clouston to regard it as a dangerous hypnotic, but found on going to Paris, it was very extensively used there, and regarded as perfectly safe. By some of our authorities it was still regarded as dangerous, and that it should be expunged from the list of hypnotics.

With regard to the second variety of insomnia, that in which the patient wakened in the morning—the best drug was veronal. He did not administer it in larger doses than 10 or 12 grs. Its action was not so immediate as paraldehyde, but it was much more prolonged, It was a useful drug in melancholic cases. Such patients waken early. and not only were they most depressed early in the morning, but it was a favourable time to commit suicide. Melancholic patients treated at home therefore for safety, require hypnotic treatment of this kind. It did not produce many serious effects, although he had seen one or two cases in which it produced irregularity of the heart's action. He had known of patients taking it for prolonged periods.

There was another measure, which Professor Cushny had scarcely referred to—that was suggestion. He believed it played an enormous part in sending people to sleep, and also in producing insomnia. He had experience of this, not only by direct suggestion, but in a very large number of cases by indirect suggestion. He had treated scores of melancholic patients, who had continued to receive a few drops of paraldehyde in water for long periods in order to produce sleep. They were greatly distressed if they did not get their medicine, but it was obvious that the few drops of paraldehyde was not the cause of them sleeping. He had recently had a patient, who had taken from 15 to 20 grs. of veronal every night for about four years. She had got into a condition somewhat resembling that of a drunkard, unable to settle to anything and neglectful of her person and duties. The amount of veronal was gradually reduced, and then with a good deal of suggestion she was placed on another drug, which she was told was equally powerful. This was done by adding salicine and lactate of calcium to the veronal. The veronal was then gradually abstracted, and now this patient, who for four or five years required these large doses of veronal, had now slept every night for three months on salicine and lactate of calcium. Nothing in the world would induce her to give up her powders. Could there be a more powerful illustration of the influence of suggestion? If suggestion can operate in this way in a person suffering from chronic insomnia, how much more powerfully would it operate in an ordinary case of sleeplessness? In the case of children the effects of suggestion in producing sleep should never be forgotten.

With regard to the use of sulphonal about which there was such differences of opinion, he regarded it much more as a sedative than as a hypnotic. It was ideal in two of its qualities—namely, the absence of taste and its prolonged action. It should always be given dissolved. It is very soluble in very hot water, but only 2 grs. will remain in solution in an ounce of warm water. As Dr Ker had told them, he had given up the use of it for very many years. He had

since discovered that the fatal case, which determined this action, had received from the nurse much more sulphonal than had been prescribed. He had an anxious feeling whenever he employed it, but he thought if the bowels were kept open and the urine examined spectroscopically and the sulphonal given dissolved, it was fairly safe. Where a combined action as a motor sedative and a hypnotic was desired, it was very useful.

Professor Edwin Bramwell said that the physician was consulted from time to time by persons suffering from insomnia, and that the symptom was one which the medical man was constantly called upon to treat in cases of illness of various kinds. Insomnia he thought might be defined as an inability to sleep, despite the need for sleep and the wish to sleep. Sleeplessness was sometimes a very grave symptom. All practitioners of experience would probably agree that they had seen cases of acute disease in which insomnia had been a potent factor in determining death, and other cases in which the drug habit had been acquired as a consequence of sleeplessness. Individuals differed greatly in the amount of sleep they required. The man engaged in a strenuous vocation who was able to do with little sleep without detriment to his health, and who had the gift of dismissing his mental pre-occupations and falling to sleep at a moment's notice, was to be envied.

Etiological factors of various kinds had been referred to by the previous speakers. The satisfactory treatment of every case of insomnia depended upon the detection and correct appreciation of its cause. This was usually apparent in the large group of cases in which the insomnia was due to pain or bodily discomfort, or in which it was associated with febrile disturbance. Idiosyncrasies in relation to articles of diet and to drugs had to be borne in mind. A case in which sleeplessness was attributable to tobacco, a not very common cause of insomnia, had its humorous side. A busy lawyer who consulted the speaker because of insomnia, said that he had been a bad sleeper for a number of years. It was ascertained that the patient was a heavy smoker, while he admitted that on one occasion some years previously he had given up smoking for six weeks, and that during this period he had slept well. No other cause for the insomnia could be found. When it was pointed out to him that tobacco was probably the cause of his sleeplessness, and that it would be wise to reduce his weekly allowance, the patient's reply was to this effect: "I did not come to you to be told that it was tobacco which was the cause of my insomnia, for I knew this, but I consulted you because I thought you would do something to cure my sleeplessness." Nervous exhaustion and mental pre-occupation were often responsible for insomnia. Professor Cushny had, from personal experience,

advocated the advisability of reading an unexciting book for half an hour or so before going to bed; the writer had found this simple procedure of the greatest value in cases of the kind just referred to. Physical exercise had also been mentioned by Professor Cushny, but a word of warning was called for in this connection, for, while exercise was undoubtedly most useful in helping to promote sleep in the case of some of those sufferers from insomnia, who were in other respects healthy individuals, the speaker was quite satisfied that exercise often accentuated the sleeplessness when this symptom was associated with exhaustion of the nervous system. Anxiety and worry were common causes of insomnia, and it was in cases of this kind in which the worry could not be removed, that the danger of the drug habit was most to be feared.

What was to be done in a case of insomnia in which the nursing methods, as Dr Ker had termed them, failed? It was interesting to note that whereas Professor Cushny had said little regarding the use of hypnotics, and had indicated that drugs were to be employed only as a *dernière résort*, Professor Robertson and Dr Ker had devoted their remarks for the most part to a summary of their experience as to the relative value of some of the medicinal agents employed in producing sleep. It was to be remembered, however, that the last named speakers were referring to a different type of case, in which severe mental or febrile disturbance was the determining cause of the insomnia. Professor Cushny had advocated the claims of chloral as an hypnotic, and had stated that there was no pharmacological evidence to show that this drug had a really depressing effect upon the heart. The speaker recalled the case of a man suffering from spasmodic torticollis, who was kept constantly under large doses of chloral for ten days, and wakened only for his meals. At the end of this period, although the torticollis showed no improvement, the patient appeared to be none the worse of his experience. The way in which various hypnotics had come into and gone out of fashion was of interest. In this connection the speaker was reminded of an experience he once had while fishing on a Highland river. The fisherman upon the beat in question had a favourite fly of his own invention. Before anyone had been fishing on the beat for long, the old man would say, "Put on the Donald Ross," and it was the Donald Ross which caught more fish than any other fly on that river. While alcohol had to be prescribed with caution in the treatment of insomnia, there could be no doubt as to its value in certain cases. Many years ago a physician, who in his day was one of the leading consultants in London, had told the speaker that he considered a bottle of stout at bedtime an invaluable remedy in the treatment of many cases of insomnia. Professor

Bramwell had had repeated opportunities of corroborating this statement.

The distinction between the two types of sleeplessness to which reference had been made—the inability to go to sleep, and the early waking with inability to sleep later—was an important one. Insomnia of the latter type was often dependent upon an over-fatigued or over-active brain, or was a sequel to prolonged illness, notably influenza. As Professor Rutherford used to say, "In the early morning hours the vital tide is at its ebb." A biscuit or some hot milk or Benger's food were often invaluable remedies in producing sleep in these cases.

No reference had been made by the previous speakers to habit sleeplessness. Sleep, it was to be remembered, was a more or less automatic spontaneous function which might be interfered with by various causes. The relation of the mental factor to sleeplessness was often a question of importance. Sleep might be interfered with if the attention was concentrated upon the function, just as was the case with some of the other autonomic functions of the body, for example, the action of the bowels. Some individuals who had paid much attention to their ability or inability to sleep believed erroneously that sleep in their case was only possible when certain conditions were complied with, just as others by a process of quite erroneous reasoning were apt to think that certain articles of diet produced in them digestive disturbance. Anxiety regarding sleep amounting to the fear of insomnia was indeed a not uncommon cause of sleeplessness. The interposition of the attention was a factor in producing sleeplessness which was not sufficiently realised. When a habit insomnia was set up a variety of symptoms might result which in their turn accentuated the sleeplessness. The vicious circle must be broken at all costs and hypnotics were often here a necessity. There was no danger of inducing a drug habit under such circumstances if the physician kept the treatment in his own hands, and the somewhat prevalent misconception that a drug sleep was undesirable in that it was not natural sleep must be explained to the patient. In cases of this class the patient must not know the drug or the dose he was taking. The hypnotic might be given in cachet form, and the dose gradually reduced until natural sleep was regained.

Finally, in the treatment of every case it was necessary both to attempt to picture the effects of the insomnia and to try and realise the causal factor or factors responsible for the sleeplessness.

Dr R. A. Fleming pointed out that the usually accepted theory of the state of the brain in sleep was a requisite degree of anæmia, not of course an excessive anæmia which led to insomnia, but that any condition predisposing to congestion of the brain

interfered with sleep. This conception of the brain during sleep aided the physician greatly in an attempt to cure many cases of insomnia without drugs—a pillow added or a pillow taken away often proving effectual. He agreed that in every case of insomnia an attempt should be made to find out the cause and to remove it before hypnotic drugs were restored to. Dr Fleming stated that the drink of hot milk or beef-tea which is believed to render the too active brain sufficiently anæmic by removal of blood to the stomach must, to be successful, be carried out in the most careful way. It must not be drunk until the patient is in bed and ready to try to go to sleep. The patient must not get up to turn off gas or electric light, but must have a light at the bedside which can be easily extinguished. Then, after the hot drink, he should put his head on the pillow at once. Possibly an element of suggestion enters into this simple method of treatment and aids in its effectiveness.

Dr Fleming mentioned two personal experiences which produced insomnia. Although, as a rule, a good sleeper, a night spent in a tent, during his war experiences, when the wind was high, absolutely precluded sleep, due unquestionably to the constant stimuli of creaking ropes, etc., which reached the brain. A second experience which helped him to accept what Professor Robertson had just said, that sleep deep at first got less and less profound towards morning, was, that when learning to drive a motor car he always woke up in the early morning afflicted with horrible dreams of the car running backwards down a precipice, while the driver was totally unable to find the handbrake.

As to the method Dr Fleming found of greatest service in courting sleep was a suitable preparation for sleep. He advocated reading in bed some form of literature which was already familiar but which turned the mind away from all day worries, and instanced Sir Walter Scott's novels as suitable literature. No exciting novel or book which is controversial should be selected. Professor Cushny stated that financial problems were not suited to induce sleep, but Dr Fleming held that a really pleasant financial problem—not an income tax return—had often proved highly soporific in his own case.

In conclusion he advocated as the best hypnotics of all those mentioned, paraldehyde in 3-drachm doses (for an adult) and heroine. The former was of exceptional service in pneumonia, and the latter where a hypodermic drug was necessary.

Dr Keppie Paterson referred to the fact, that tea or coffee late in the evening prevented his sleeping, and he found in general practice that fully one half or nearer two-thirds of his patients were similarly affected. He therefore prohibited tea or coffee after 5 P.M., and in very bad cases at any time in the day. The fear of inability to sleep seven or eight hours was also an element in his insomnia

until he found that he could often get along fairly well with five and a half to six hours' sleep. There was something in the degree of sleep we obtained. He had recently found 10 grs. of iodide of potassium at bed-time gave him a good sleep. In neurasthenic women, a mixture of hydrobromic acid with small doses of chloral given thrice daily seemed to take the edge off their nerves and allowed them to sleep.

Dr Torrance Thomson said, in discussing the treatment of insomnia, it would appear to be desirable to have some theory of what sleep really is. It is suggested that the psychological conception of sleep may prove helpful. According to this conception, sleep is a response to a psychological necessity. Reality can only be endured on condition that we can escape from it at regular intervals and for considerable periods of time—equal to about a third of each day.

The new-born infant obviously resents being born, has no relish for reality, and is only satisfied when it has been persuaded into imagining that it has resumed its antenatal state of peace and omnipotence.

All sleep is a symbolic return to the mother's womb. The technique of sleep and all devices for inducing sleep aim at effecting the accomplishment of this symbolic return by producing, as far as possible, the intrauterine freedom from stimulation.

Dr C. W. Somerville cited some experiences:—

(1) The matron of an inebriate home said she had absolutely no sleep for three nights. She was given a small bottle of paraldehyde, with the instructions:—To go to bed—if awake in half an hour to take half the bottle; if still awake at the end of another half hour to finish the bottle. She returned the bottle with the cork undrawn after a week as she had slept well every night. The certainty of sleep had removed the fear of sleeplessness.

(2) A more recent case of several nights of sleeplessness was treated by his wife lathering his scalp with soap and wrapping it up in a towel; he slept well and the soapy lather was washed out next morning.

Personally Dr Somerville found financial work, or tea after 9 P.M., kept him awake for most of the night; coffee or cocoa had not that effect.

Dr John Orr said he was not disposed to concur with the view that bromides were not sedative, but agreed with Professor Robertson that their effects were considerably enhanced by the elimination of chlorides from the diet during their administration; he referred to the absence of cardiac depression of chloral hydrate, to the stimulant

effect of paraldehyde on the heart, and suggested that larger than the pharmacopœial doses be given in acute pneumonia; he alluded to the possibility of sulphonal being of value in a diagnostic sense occasionally, and defined some of the occasions on which morphine preparations might be used in preference to other hypnotics.

The President (*Sir Robert Philip*) congratulated the Society on having the discussion opened by so eminent an authority as Professor Cushny, whom they welcomed as their guest. He had been impressed with the simplicity, clarity, and picturesqueness of the opening address, and with the fact that, far-reaching as the speaker's knowledge was regarding pharmacological possibilities, he had limited his recommendations largely to recognised physiological methods and pharmacopœial remedies.

PLASTIC REPAIR OF THE FACE AND LIMBS.*

By J. J. M. SHAW.

In presenting this communication upon the plastic repair of the face and limbs, Mr Shaw exhibited a series of lantern slides to illustrate the practice and results of two methods employed—the Thiersch graft upon a mould and the tube pedicle graft. Tribute was first paid to the influence of Mr H. D. Gillies in the recent developments in plastic surgery, and acknowledgment made of the value of an association with him in the work at Queen's Hospital, Sidcup.

The Thiersch Graft upon a Mould.—The application of a Thiersch graft wrapped around the dental composition known as "stent" was then described. The cavity to be lined is formed by dissection and complete removal of scar tissue. The dental composition is then softened by heat and pressed in to the cavity. When a firm impression has been taken, the mould is removed. A Thiersch graft is cut from the arm in the usual way, is wrapped round the mould with the raw surface outwards and so inserted. When the cavity is large or irregular, two or three graft strips, slightly overlapping one another at the edges, should be employed to avoid wrinkling and unequal tension. The graft is maintained in position by cross suturing at the eyelids, by a dental cap splint and bracket in the mouth, and by a dental splint with

* Read 7th March 1923.

FIG. 2.

FIG. 3.

FIG. 1.

FIG. 4.

FIG. 1.—Arterial pedicle for nasal and lip defect. (1) Delimitation on forehead: (2) Partially raised: (3) Tubed and implanted (lip suture incomplete): (4) Portion returned to forehead; free graft to gap.

FIGS. 2, 3, and 4.—Sub-total Rhinoplasty by forehead arterial pedicle, for gunshot wound. Photographs show profile before and after operation, also recent "lay" photograph. Pedicle fashioned similarly to case shown in Fig. 1.

Operative Stages.—(1) Excision of scar tissue and restitution to proper position of right ala which had been allowed to heal faultily. Subcutaneous implantation of slip of costal cartilage in vertical position at root of nose. (2) Lining of nose formed by turning down skin over root of nose along with embedded cartilaginous support. Covering supplied by forehead arterial pedicle similar to that shown in Fig. 1 for another facial defect. (3) Portion of pedicle returned to forehead. Gap remaining on forehead covered by whole thickness skin graft from abdomen.

an ascending arm for the nose. Photographs of illustrative cases were shown indicating the usefulness of the method in ectropion of the eyelids, in adhesions of the labio-gingival sulcus which prevent the fitting of dentures, and as an intra-nasal lining in deformities caused by lupus, syphilis, and certain types of old-standing trauma.

Reference was made to the necessity of supplying in these types of nasal deformity a new cartilaginous framework, angled at the tip of the nose and supported both at the upper end and at the spine of the maxilla, in addition to the restoration of the lining. In all cases a temporary improvement can be effected by the insertion of a simple straight slip of cartilage; but it is only in a condition of comparatively recent trauma in which no intra-nasal lesion of an ulcerative type has existed, that a permanently satisfactory result can be attained by a cartilage which is supported by bone at the upper end only.

In certain cases of deficiency or scarring of the conjunctiva, after removal of the eye, which prevent the insertion of a shell, the defect may be remedied by a Thiersch graft. Where injury of the orbital plate has occurred with marked sagging of the whole socket, extirpation of the conjunctiva and ciliary margins with suture of the skin edges is the most satisfactory procedure. An eye-shade is subsequently worn.

The Tube Pedicle Graft.—The two varieties of pedicle grafts, to which were given the distinguishing names of "anastomotic" and "arterial," were next demonstrated. In the former, most commonly fashioned upon the neck or abdomen, three operative stages are required. By two parallel incisions and undercutting between them, a strip of skin of the required length is raised and formed into a tube by suture of its free edges. The ratio of breadth to length should be approximately as one to three. The subjacent platysma in the neck, and a thin stratum of fat in the abdomen are raised along with the skin to form a core for the tube. Both ends are left attached and the skin edges bordering the raw area from which the pedicle has been raised are drawn together and sutured beneath it. By daily constriction of the end which is to be first freed, the anastomotic channels of the other end are developed.

Three weeks after the first operation, the pedicle is divided at the end prepared for separation, partially opened out and

implanted at a suitable margin of the new bed. After the lapse of another three weeks, the remaining original attachment is set free and the pedicle opened throughout its whole length to completely fill the defect. The length and flexibility of the pedicle obviates the need for fixation of the parts by plaster in the intermediate stage.

In the arterial type the operation is carried out in two stages. The most common example is the forehead flap in which the pedicle contains the anterior branch of the superficial temporal artery. The extent of the facial defect is measured upon the forehead by means of a pattern of tin-foil. It is demarcated by incision on three sides, the fourth being left continuous with the stalk which is outlined by parallel incisions stretching downwards and outwards to the zygomatic region. The flap is then raised by dissection from the forehead and care must be taken to avoid injury to the contained artery especially towards the base of the pedicle. The pericranium is left intact. Owing to its dependable viability, the implantation of the freed end on to the facial bed can be effected at once and, a fortnight later, the second stage is carried out by the return to the forehead of the proximal part of the pedicle which has served as a conduit. In the interval the raw area on the forehead is dressed with "ambrine," and the gap which remains after the second stage, corresponding to the portion of skin now implanted on the face, is covered by a whole-thickness free skin graft from the abdomen or by local advancements of the scalp. A lymph œdema of varying degree appears in the facial graft on the second day after the severance of its pedicle. Its disappearance is accelerated by massage and usually takes place within three weeks.

Examples were shown of the treatment by the forehead flap of facial disfigurements due to burns, port-wine stains unsuccessfully dealt with by other means, lupus excision, and gun-shot wounds. In chronic ulceration and cicatricial contractures of the arms and hands, the employment of the abdominal anastomotic pedicle was illustrated. In these situations, the tube pedicle was considered to be the most effective method of plastic repair. For the lower limbs, the pedicle graft, whether obtained from the sound limb or from the abdomen by successive "caterpillar" stages, was not advocated until it became evident that healing could not be effected by splintage and rest or by free grafting.

Discussion.

Sir Harold Stiles said the Society was deeply indebted to Mr Shaw not only for the splendid work he had brought before them but also for the admirable manner in which he had presented so difficult a subject. After the appalling destruction of life, mutilation, and disfigurement for which the War was responsible, it was some consolation to feel that it had been the means of bringing about great advances in certain departments of surgery, and in none more than that with which Mr Shaw had so ably dealt. Not a few of these advances had been made by young surgeons who had concentrated their keen, plastic, and resourceful minds on the new surgical problems which the War had brought into prominence. Mr Shaw had boldly tackled one of the most difficult of these problems, and the demonstration which he had given to-night showed that he had taken full advantage of the opportunities which the work at Sidcup had afforded him and that, thanks to his aptitude, ingenuity, and skill, he had made himself a master of a branch of surgery of which the ordinary surgeon, owing to want of experience, had comparatively little knowledge. He (Sir Harold Stiles) felt proud to think Mr Shaw was an Edinburgh graduate; by the work he had done he had made himself a valuable asset to our School, and it was to be hoped that every facility would be afforded him for practising and teaching the art of plastic surgery.

Dr Douglas Guthrie said that no one who had any experience of this branch of surgery could fail to appreciate the excellent results secured by Mr Shaw in those very difficult cases. He (Dr Guthrie) had used the Thiersch graft on a mould, in a case of radical mastoid operation with a satisfactory result. His experience of complete rhinoplasty was small, and his principal difficulty had been to secure a satisfactory columella. This part of the flap was very apt to slough, and he should be glad to hear how Mr Shaw sought to avoid this accident. He had reconstructed the bridge of the nose by cartilage grafting with success in a number of cases of deformity following injury, but in cases of syphilis had usually found that the entire nose was so shrunken, owing to absorption of its bony supports, that a satisfactory result could not be guaranteed. He had not, however, adopted the ingenious method of providing a new lining which Mr Shaw had described. Lastly, he thought that a few remarks from Mr Shaw on the subject of anæsthesia would be interesting and helpful.

Mr Wade said that it was his good fortune to have Mr Shaw as one of his surgical colleagues in the Ministry of Pensions Hospital, Craigleith. He had witnessed Mr Shaw operate on a number of cases there, and had been able to observe their progress from day to day. The impression he had formed was that the region where plastic

surgery found its greatest usefulness was in the face and neck. To carry out such work as Mr Shaw had so brilliantly done required a combination of qualities that were only occasionally met with in one individual. He must first of all be a sound, general surgeon with an accurate knowledge of the broad principles of general pathology, and have in addition many of the qualities of the artist and the architect. At the same time, it appeared to Mr Wade that there were many departments of general surgery where the plastic surgeon could give great assistance. Although a case they had had together where an attempt had been made to cover over a large chronic ulcer of the leg by a graft of the entire thickness of the skin had not proved a complete success, he thought that further attempts to achieve this were warranted, as these cases were so difficult to treat, and not infrequently ended in the limb requiring to be amputated.

There was another field in which plastic surgery might be well employed, and that was in the case of the recent accident where a large portion of skin had been permanently removed from such a position as the palm of the hand. In such a case there came a time, usually within two or three days after the accident, when the wound could be considered surgically clean, and the risk of infection developing might be considered as passed. At this stage plastic surgery would be of great assistance in making good the defect by a whole skin pedicle graft before cicatrisation, and the deformity to which this gives rise had developed.

Mr Pirie Watson expressed his admiration of Mr Shaw's work in plastic surgery applied to facial disfigurements and limb deformities. His own experience of whole thickness skin grafting was limited to deformities of the hand due to scar contracture following burns and septic lacerated wounds. His interest in this direction was first stimulated by Professor Alexis Thomson, who has successfully transplanted flaps of abdominal skin by the "pedicle" and "bridge" methods, in several cases of scar contracture of the hand following burns, with great improvement in function. In his own cases—three in number—one scar contracture of the hand following a burn, the other two contracture of the hand following septic lacerated wounds, he used the "pedunculated" abdominal skin flap, which was at once stitched on to the hand after excision of the scar tissue, *i.e.*, without the intermediate stage of forming a "Tube." In these three cases the grafting was successful and the improvement in function very pleasing. The "Pedicle" method compared with the "Tube" saves three weeks in time and lessens by one the number of anæsthesias required to complete the operation. Where the vitality of the graft is uncertain the Tube method is to be preferred. He agreed with Mr Shaw that the thigh is not a suitable source for a tube graft. In a recent case he tried a tube graft from

the thigh of a boy aged 11, but the central portion necrosed, and the attempt was abandoned.

Mr Shaw replied to the points raised in the course of the discussion.

In the nasal deformities due to syphilis, the chief factor is the backward traction exerted by the parts which have been the seat in the early stages of a muco-cartilaginous ulceration and necrosis, and there is seldom an actual shortage of covering skin. Such a disfigurement can therefore be remedied by a restoration of the lining after removal of the obstructive fibrous tissue, supplemented at a later date by the provision of an adequate cartilaginous support.

Where the coverings are also affected, a rare condition with modern anti-syphilitic treatment, the forehead flap is the only available method of restoration. The chances of failure in these cases should be borne in mind and expressed to the patient before the operation is undertaken.

By the use of two small divergent processes at the end of the main flap in the operation of rhinoplasty, the difficulty in the construction of the columella is largely removed. On moulding the nose in its new situation and shape, the raw surfaces of the processes are opposed to one another. On suturing, a complete columellar tube is thus formed, so that the raising of a lining flap from the upper lip, a very unsatisfactory procedure, is rendered unnecessary.

In regard to anæsthesia, the use of intra-tracheal gas and oxygen is much the most satisfactory method both for patient and surgeon.

In the chronic varicose ulcer of the leg, an attempt at closure by rest and multiple epithelial plants is a sounder procedure than the employment of a tube pedicle as the same circulatory defects which induce and perpetuate the ulcer are probably present upon the hitherto sound limb.

For the recent injury of the hand with loss of skin covering, nothing could be suggested in addition to the thorough cleansing already performed. When the final amount and shape of skin required became obvious in the course of a few days, an abdominal pedicle could be cut which would be ready for use when the bed was sufficiently healthy for its reception.

The thigh pedicle which had become attenuated at one point was likely in the end to give a satisfactory result, as the factors favourable to a successful free graft were present with the addition of a small additional blood supply and channel of lymph escape. Thigh pedicles are particularly prone to give occasional disappointment on account of the presence of an area of anastomotic weakness at the junction of the middle and lower thirds of the thigh. The same difficulty is also experienced in pedicles and flaps which traverse the level of a joint or cross the midline of the body at any point below the level of the chin.

THE BENEFITS OF ORGANISATION IN THE TREATMENT OF LUPUS.*

By ROBERT AITKEN, M.D., F.R.C.P., Clinical Tutor, Skin Department, Royal Infirmary.

THE intractability of lupus vulgaris is well known. So marked, indeed, is its obstinate and chronic nature that the statement is sometimes made that lupus is an incurable disease. The difficulties of treating the condition are enhanced by the lack of control over the patient, who attends irregularly as a rule, and not infrequently neglects all forms of treatment for months at a time.

In July 1914 Sir Norman Walker read a paper before the Dermatological Section of the British Medical Association, the title of the paper being, "The Need of Greater Method in the Treatment of Lupus." The outbreak of war prevented anything being done immediately, and it was not till well on in 1919 that practical expression could be given to the views set forth in the paper mentioned.

Prior to September 1919 the cases of lupus had been seen here and there among other diseases just as they came up. In that month arrangements were made for all lupus cases who could conveniently manage, to come to the hospital on a given day. Wednesday afternoon seemed to be the most suitable time, and the patients were accordingly informed, so that now there are about 120 patients with lupus who attend regularly at intervals of a week or two weeks, or as frequently as their condition demands. In the case of patients who stay at a considerable distance from Edinburgh the interval is usually one month.

By having an arrangement of this nature it is possible to make more accurate comparisons of the value of any particular remedy, as one set of patients can be treated with this substance, and another with that. This is useful from the point of view of the physician, but the lupus clinic has another and more important value, and this is the effect on the patients. The fact that the physician takes the trouble to come to the hospital at a time when patients are not usually seen, and to have patients all suffering from the same disease, makes them feel that more interest is being taken in their

* Read 2nd May 1923.

condition. This, perhaps, makes them a little more willing to co-operate with him, and that, of course, is all-important. But there is another and more important aspect, and that is the moral effect which such a clinic has on the patients attending. The new patients see others who have been under steady treatment and who have improved, and they also see others who have neglected treatment and whose condition is so repulsive to all who are not familiar with the more advanced stages of the disease. These two pictures make the new patients anxious and eager to co-operate in the treatment, the first by holding out hope of improvement, the second by the dread of being so disfigured.

All the patients who attend the clinic have fully explained to them the chronic nature of the disease, and the need for steady treatment. It is clearly pointed out to them that it is the physician in charge and not they themselves who must say when attendance is no longer necessary. A roll is kept and each time a patient attends he has a mark put against his name indicating that he has been seen, and the date fixed for his next visit is also noted. If he fails to put in an appearance on the day indicated, a red mark is placed against his name. If he does not attend the following week or the week after, a postcard is sent intimating that he must attend. In this way a certain amount of control can be exercised.

Possibly we, as a profession, are much to blame for the want of regularity in the attendance of patients with lupus. We are rather apt to shirk telling them how long the disease is likely to last. We may say, "This is going to take a long time to get well," but patients differ in their conception as to what a long time is. Some think three months a long time, while others think one month long enough if they do not see any improvement. It might be wiser to tell a patient with a patch of lupus the size of a shilling that the disease will not be cured for at least a year and may take even longer. It may stagger the patient at first, but he will appreciate the information later when so little improvement is observed after the lapse of two or three months.

Another advantage of treating at the same time a large number of patients suffering from the same disease is the ease with which other investigations can be carried out. It has been suggested that a large proportion of the population, apart from

known cases of syphilis, show a positive Wassermann reaction. About two years ago the Wassermann reaction of all the lupus patients at that time attending the clinic was tested. The observations were carried out by Major Coullie, I.M.S. Altogether 63 patients were examined. Of these 5 were returned as positive, all the rest negative. Of the 5 positives one had scars of an old syphilitic rash, a second gave a history of miscarriages, and four years before the reaction was taken a note was made on her card that the lesion did not all appear to be tuberculous. In a third case the diagnosis was clinically doubtful. We have then two positive results in cases where there was no definite specific history, though in one of these the destruction of the nasal tissues suggested syphilis rather than tubercle. But even counting this case, there are only 2 cases out of 63 in which a positive reaction was returned, and no definite history or clinical evidence to suggest it.

These figures do not support the contention that there is a large number of positive Wassermann reactions among the general population, or at least the statement does not seem to apply in this neighbourhood.

The treatment carried out at the lupus clinic has been similar to that employed at other hospitals in the treatment of this disease with the exception of one item. We use carbolic acid, trichloracetic acid, lactic acid, acid nitrate of mercury, and X-rays. Sometimes keloid has followed the continued use of trichloracetic acid and acid nitrate of mercury. It has seemed to be more frequent after the former, but this statement must be taken with the reservation that trichloracetic acid has been used more than the mercurial preparation because it appeared more beneficial.

X-ray treatment has been sparingly employed on account of the risk of carcinoma, but sometimes the rays can be used with good effect.

Not infrequently the catarrhal element in the disease is rather troublesome. If it is very marked, the sharp spoon is probably the most satisfactory method of dealing with it. In most cases, however, this is not necessary, and yet the catarrh is sufficient to interfere with the other remedies applied. In such a case it is of advantage to administer a staphylococcal vaccine, 25 millions every week for three or four weeks usually being sufficient to bring the catarrh under control.

I now come to the part of the treatment which is not so usually administered. I refer to injections of tuberculin. So many experienced dermatologists have tried and discarded this remedy that it is with diffidence I approach the subject. Yet with all confidence in its value I enter a plea for its more general use. Before the war Koch's tuberculin was the one employed in the Skin Department, some cases getting New Tuberculin (T.R.) and others getting the Original Tuberculin (O.T.). These latter were admitted to the ward for a few days till all reaction had passed away. In 1913 one or two patients were treated on a more intensive system, Perlsucht Tuberculin Alt (P.T.O.) being the type of tuberculin used. It was found after treating a few cases in the wards that, with careful administration, it was possible to give it without a reaction occurring, and it was then decided to treat out-patients in this way. About a dozen patients were so treated in 1914-15 with encouraging results. Then the stocks of German tuberculin ran out, and we had to resort to British varieties. None of these at that time available gave satisfactory results. This part of the work had then to be given up, and it remained in abeyance till the institution of the lupus clinic.

Since then, treatment with tuberculin has been steadily carried out, and at the present time there are as many as 46 patients being so treated. Some receive injections every week, others every fortnight, the interval being governed to a great extent by the distance the patient has to come to hospital. Whether or not the treatment is regarded by the patients as beneficial is shown by the regular way they come up for their injections. Several during the winter have remarked that their condition has never been so well before during the cold weather, and some have spoken very favourably indeed of the treatment. Better than words, however, is the exhibition of photographs of the condition of the patients before and after the treatment.

I do not claim that tuberculin benefits every patient. Some do not improve under its administration, but this holds with practically every remedy we possess. In some cases, while it does not cause improvement of itself, it seems to render the patient more amenable to treatment by other remedies, and in this way an indirect benefit is conferred. I firmly believe that tuberculin is one of the best remedies we possess and have no hesitation in giving it to a patient, especially if the disease is at all extensive We must not expect miracles from it, and

its use ought to be continued not for two or three months but for at least a year. We have not yet obtained *THE* remedy for lupus, and meantime we must work patiently and perseveringly with all the means at our disposal till more is understood of the factors underlying and governing the disease.

The lupus clinic has been in existence now for three and a half years. The initial enthusiasm has had time to work off, and a sufficient period has elapsed to allow the results to be observed and judged. I think it may safely be said that the clinic has justified its existence and the time which has been spent on it. The patients approve of it, and the best testimony they can give is the regular way in which they attend week by week the whole year round. The results have, on the whole, been good, most of the patients improving, some considerably. Quite a number have been discharged cured, but are asked to report themselves at intervals. Instructions are given to them to return at once if they see even a small spot which they think suspicious. This advice has been followed, several of the patients having come back with a tiny spot showing, while others have returned thinking a part suspicious, but no disease being found on examination. It is a useful practice to keep a note of the cures apart from the reference on the patient's card. In this way the actual figures can be available at once to correct, if need be, one's impressions.

The cures before and after the institution of the clinic are interesting and instructive. From the beginning of 1915 to the end of 1922, 288 new cases of tuberculosis of the skin came to the Skin Department. These figures refer only to Sir Norman Walker's department. Dr Gardiner kindly offered to place his statistics at my disposal, but as the lupus clinic refers solely to Sir Norman's patients, it seemed better to take his figures only for the purpose of comparison. Of these 288 cases only 8 were discharged cured, 2 were apparently cured but did not return after a sufficient interval to allow one to say with certainty. Even counting them, however, only 10 cases were cured apart from the clinic. Of the cases which have attended the clinic since its inception 26 have been discharged cured, several more have shown no sign of disease for some months, but are being kept under observation for some time longer, as is the usual custom, before being told that there is no need for further attendance. These figures point strongly to the value of the clinic.

FIG. 1.

FIG. 2.

FIG. 3.

FIG. 4.

FIG. 5.

FIG. 6.

One must confess, however, that in some cases the results are not encouraging. No matter what treatment is carried out, no improvement is effected, and sometimes the condition deteriorates in spite of treatment. Even when the patient is

Fig. 7.

Fig. 8.

only too willing to assist, and when the general condition is all that could be desired, one is unable to report improvement. There is still a large field for research in lupus.

Fig. 9.

Fig. 10.

Case I. (L. D.).—This patient gave a history of intranasal trouble before the skin disease began on the lower part of the nose in 1909 when she was 17 years of age. The disease spread rapidly and two spots appeared on the right cheek. About a year later she came to the Skin Department, but before receiving treatment she was sent to

have her intranasal trouble dealt with. As the result of operative treatment for this, the skin lesions improved. The spots on the cheek were frozen with carbonic acid snow about a month after the operation. The result was excellent, and these spots have not troubled her since. During 1911-12 she had X-rays, carbonic acid snow, and T.R. injections. At the beginning of 1913 she was admitted to the ward for O.T. injections, and after eleven months' steady treatment a considerable improvement resulted as shown by Figures 1 and 2. During the war this patient went to London and had persistent treatment with the Finsen light and is now cured.

Case II. (M. L.).—This patient was 6 years old when the disease began in 1905, and it spread rapidly as she was rather neglected at home. She came to the Skin Department first in 1911 and her condition was so bad that she was admitted to the ward at once. She remained there for ten weeks, and under X-rays, oleate of mercury ointment, and T.R. injections there was a marvellous improvement.

She did not attend during 1912, but came regularly in 1913 when she was given O.T. injections. In March 1914 she was in the ward for four months while getting the intensive tuberculin treatment. Figures 3 and 4 show the improvement which resulted from the steady treatment during 1913-14.

Case III. (D. B.).—In this case the disease began on the right cheek in 1908 when the patient was 7 years old. It had been scraped and X-rayed before she came to the Skin Department in 1911, but the disease spread in spite of this treatment. She had X-rays and carbonic acid snow during the first year of her attendance, but she had to be admitted to the ward because the condition became so catarrhal. During her three months' stay in hospital great improvement was effected. She had T.R. injections after she went out, but the want of attention at home did not give any treatment a proper chance. In spite of this, however, she continued to improve as shown in Figure 6. During the war no treatment at all was carried out and the disease spread to the extent shown in Figure 7, which was taken on the institution of the clinic. She has attended there regularly and Figure 8 shows the improvement which has been effected. This is almost entirely due to tuberculin, as only the edges have been painted with trichloracetic acid.

Case IV. (A. M'G.).—This boy was 9 years old when the disease began in 1911 on the upper lip. When he came to the Skin Department in 1912 it was rather extensive; it was on the nose, upper lip, right cheek, gums, and on each side of the neck below the ear. After the first attendance he did not return for six months, then there was one attendance and a lapse of four months. When he did return he

received a few X-ray exposures, but the disease spread in spite of this treatment. He then received tuberculin injections, and marked improvement resulted. Unfortunately, in this case also, nothing was done during the war, with the usual spread of the disease. He was asked to attend the clinic on its institution, when his condition was as shown in Figure 9. He has attended on the whole regularly, receiving tuberculin injections and having the edges painted with trichloracetic acid. The improvement is shown in Figure 10.

Case V. (Mrs M'F.).—In 1904 when this patient was 13 years old a patch of lupus appeared outside the left nostril and spread in spite of scraping and X-rays. In 1906 the right nostril was attacked and soon afterwards a patch appeared on the right cheek. She came to the Skin Department first in 1910 when it was found that there was intranasal lupus in addition to the skin lesions mentioned.

The intranasal disease was dealt with thoroughly, and the skin condition treated with some success, but towards the end of 1912 a patch appeared on the right side of the chin. It was then decided to give her O.T. injections, but owing to family circumstances she did not attend regularly in 1913-14. During this time practically nothing was done, and the disease spread. She returned in November 1914 and was put on the intensive tuberculin treatment, to which she responded very well. Improvement was rapid, and, aided by her removal to the country just outside Edinburgh, continuous. She is now cured.

Case VI. (A. B.).—At the age of 12 this patient developed lupus on the nose. After being treated elsewhere for a year she came to the Skin Department in 1905, the tip of the nose and the upper lip being affected at that time. She had X-rays at intervals till the beginning of 1907, then she did not return till the end of 1908. During the next two years she used an oleate of mercury ointment and had some T.R. injections. Thereafter she had O.T. injections and X-rays with lapses from all forms of treatment till the institution of the lupus clinic. She attended there regularly and was treated entirely with trichloracetic acid, the nodules being drilled out with a sharp glass rod. She is now quite cured.

Case VII. (M. K.).—This patient came to the Skin Department first in 1918 at the age of 25. She had had the disease for five years and it covered the greater part of the left side of the face. She had some X-ray treatment at first, but the disease spread in spite of this, attacking the skin under the chin and the ear. When the clinic was instituted she was instructed to attend. The treatment has consisted entirely of local applications of trichloracetic acid. There has been no sign of disease now for a year, and on her next visit she will probably be discharged cured.

Discussion.

Dr Frederick Gardiner congratulated Dr Aitken on his concisely clear paper. He had seen some of the results and the photographs did not do them justice, although they were evidence of regular work. As regards tuberculin, he personally used it, recognising its successes as well as its failures. Recently he saw at Sequeira's clinique in London some excellent results with the Arc-Lamp—the cost was little and several patients could be treated at once. This acts differently from the Ultra-Violet Lamp, as the red rays penetrate blood and therefore can affect the whole system—radiation on the diseased area not being necessary or even desirable.

Sir Norman Walker wished first to pay tribute to the whole-hearted zeal and enthusiasm which Dr Aitken had devoted to the lupus clinique.

Perseverance was the most important ingredient in every method of treating lupus, and he was convinced that anyone who gave tuberculin a fair trial and did not condemn it after a two or three weeks' trial would admit its value.

With reference to the use of X-rays in the treatment of lupus, he had seen it so often followed by the development of carcinoma, that he said deliberately that they should only be used by those who knew of and appreciated their danger.

One of the most useful effects of the assembling of these cases in a clinique was the opportunity it gave the less affected cases of seeing the bad ones and so stimulating their zeal in attendance, and submission to treatment which was often painful.

THE TREATMENT OF DIABETES WITH INSULIN.

By Professor J. MEAKINS, in collaboration with W. ROBSON, C. G. LAMBIE, and H. W. DAVIES.

Professor Meakins.—In some ways our communication this evening may be considered a little premature, because there are so many things to be found out about the treatment of diabetes by insulin that future work will undoubtedly give us more knowledge. To use cinema parlance, insulin has only been "released a week," and unfortunately there has been a good deal of misconception about its rôle of usefulness. We propose this evening to give a short account of what it can do and what it cannot do, its difficulties and its dangers.

Your President has asked me to make a few introductory remarks regarding the romance of the discovery of insulin. Some years ago Scott, when attempting to demonstrate that the pancreas had an internal secretion, found a substance which lowered the blood sugar in animals. This product had a weak and inconstant action. It is possible that there was present more than one substance, one of which was an antagonistic body which raised the blood sugar. The research lay fallow till two years ago when Banting was intrigued with the question of the internal secretion of the pancreas. He went on the supposition that trypsin destroyed the internal secretion after removal of the pancreas from the body. He therefore tied the duct and allowed the pancreas to atrophy *in situ*. With these preparations he prepared an extract which definitely lowered the blood sugar in rabbits. It was soon found that it was unnecessary to resort to this procedure. I may say that the fundamental discovery was the demonstration of the internal secretion of the pancreas, which could be isolated in a crude chemical form and which would reduce the blood sugar in animals to such an extent that life was impossible.

With these few introductory words, I will leave to Mr Robson the account of the manufacture of insulin.

Mr Robson—*The History of the Pancreas down to the Point of Injection.*—At present we are using one source, the pancreas of the ox. We get as much pancreas as we can use and we

have had no reason to deal with other sources, those of the sheep and the pig. The Canadian workers under Professor Macleod have isolated insulin from certain species of fish. It is very interesting to know that two workers in Cambridge, Winter and Smith, claim to have isolated it from yeast. So far no details have been published. When we began isolating the insulin, it was considered necessary to make arrangements for getting the pancreas from the slaughterhouse as quickly as possible, and also at as low a temperature as possible. We had special tins made with a jacket surrounding them containing ice-cold water. As time went on we found that such precautions were not necessary. We now put so much alcohol into the tin. When we receive the pancreas we place it in a meat mincer and mince it three times until it is exceedingly fine, then place in absolute alcohol. At present we use industrial alcohol. It is allowed to stand in contact with this for three to four hours. After this extraction we fill it into ordinary filter papers. We get back only about five-sixths of total amount of liquid. From there we add more alcohol in proportion, one and a half volumes to one and let it stand overnight. By the next morning a certain quantity of precipitate separates out, which necessitates filtering it again. The clear filtrate is put into large five-litre flasks and is evaporated down. The insulin is rather unstable and we have to take certain precautions in regard to temperature. The pressure is reduced to 25 mm.—about $\frac{1}{30}$ of ordinary pressure, and the alcohol boils off at about 30° C. This evaporation is the most tedious part of the whole process. When it is reduced to about $\frac{1}{50}$ of its original bulk it is taken out of the flasks and allowed to stand overnight, when a good deal of the fat solidifies out and is separated off. From that point it is an easy matter. Absolute alcohol is added to the insulin liquid until we get a percentage of roughly 80 per cent. alcohol. This is allowed to stand overnight, when proteins, lipoids, etc., settle to the bottom of the basin. Then again we filter and the liquid comes through quite clear. The next morning we add more alcohol until the percentage is 93. In the meantime, the volume goes up from about a quarter of a litre to about 5 litres. That is allowed to stand twenty-four hours again, and in the meantime the insulin separates out as a light yellow solid. When we first started, we simply dissolved this product in certain solutions and used it for

animal experiments. Fortunately Dudley and Dale have greatly improved this product by turning the crude insulin into insulin hydrochloride. A lot of inorganic substances are thus got rid of. Insulin hydrochloride is an almost white substance, exceedingly potent. In the conversion of the crude insulin to the hydrochloride there is necessarily a large loss of weight.

Dr Lambie.—Samples of the product obtained after the manner just described differ in their potency. Before the material can be used for therapeutic purposes in man with any approach to accuracy and with safety, it has to be carefully standardised. Up to the present we have no means of determining chemically the amount of the active principle, and therefore we have to rely upon the rather more imperfect method of biological assay as a means of determining its power. This method has certain drawbacks, the chief of which is the individual variability of the animals as regards their response to the injection of insulin. The most convenient animal is the rabbit: it is easily handled and it is easy to obtain blood from the ear vein for the estimation of blood sugar.

The Effect of Insulin on the Blood Sugar of the Rabbit.—After injecting insulin into a rabbit there is a sharp fall in the blood sugar, most rapid during the first half-hour. When the blood sugar is reduced to between 30 to 40 mgm. per cent. convulsions begin to occur. There are great differences however as regards the level at which they appear, depending upon the animal and the dose. The usual time it takes for the convulsions to appear is between one-half to six hours. When the blood sugar falls very rapidly it reaches a very low level before convulsions begin. On the other hand, when it falls slowly they commence at a higher level. As to the character of the symptoms in the rabbit: they are of interest because they resemble those occurring in man as a result of overdose. First of all the animal becomes apparently somnolent, then as a rule quite suddenly the fore and hind limbs are extended straight out and the animal lies flat on its stomach. Presently one observes twitching about the eyes, then clonic contractions of the ears, and finally the other muscles of the body become involved and the animal passes into general convulsions. Very characteristic are the running movements observed. In its attempts at progression,

the animal, being unable to retain its balance, falls over and over first in one direction and then in the other. In addition to these movements the temperature falls considerably. There is marked pallor of the ears and it is difficult to obtain blood from them. Between the convulsions, which recur at intervals, there is general muscular weakness and the animal lies on its side in a comatose condition. Sometimes there is a temporary recovery and the blood sugar may rise above the convulsive level, only to relapse again later on. Finally tonic convulsions appear, with opisthotonus and outstretching of fore and hind limbs. Should death occur, the respirations cease before the heart and post-mortem rigor appears almost immediately in the muscles which were tonically contracted.

However, these convulsions can be easily cured by the injection of glucose, 3 to 4 grams subcutaneously. A rapid rise in blood sugar occurs, and recovery takes place within about ten to fifteen minutes. Animals, if untreated with glucose, seldom recover from convulsions.

A comparison of the curves of blood sugar in rabbits of different weights injected with the same dose of insulin per kilo, shows that there are great differences in the susceptibility of animals, the lighter ones generally exhibiting the greater fall in blood sugar. Nevertheless, animals of similar weight may also react differently to the same dose.

This question of variability in response is of importance because it applies not only to animals but to man.

If we are going to standardise insulin we must attempt to overcome these differences in individual susceptibility. This is partly accomplished by using at least three animals of approximately the same weight. It is of great advantage to use animals whose reactions are known by previously testing.

Technique.—Starve rabbit for twenty-four hours. Dose injected in volume 2 c.c. subcutaneously, and blood sugar estimated immediately before injection and again after two hours, and four hours if convulsions have not occurred.

Standard.—The dose of insulin which produces convulsions within four hours in a rabbit of 2 kgm. weight or one which will reduce the blood sugar to about 40 mgm. per cent. within four hours is called one "rabbit dose." This was the unit originally employed in Toronto, but the Americans, using another method (non-convulsive doses) adopted a unit which

is about four times less than the Toronto figure. Therefore one rabbit dose equals 4 of the present units. The average human dose is 10 units.

Blood Sugar in Man.—Glucose alone on the blood sugar in man. When glucose is administered to man by the mouth in a dose of 1 gram per kilo of body weight, it produces a rapid rise in the blood sugar during the first half-hour, followed by a fall reaching the normal level within two hours, and then sometimes going below it. When the same amount of glucose is given to a diabetic, there is quite a distinct delay before the rise takes place. The maximum is attained at a later period—about four hours—and is at a much higher level. The fall then takes place very slowly, requiring several hours to regain the original level.

Insulin alone on Blood Sugar in Man.—When the fall in the blood sugar in the normal individual after a dose of insulin is compared with that in the diabetic after a similar dose, it is found that in the case of the latter the drop is much greater. Moreover, in the diabetic there may be very little diminution in the blood sugar during the first half-hour following the administration, after which the fall becomes much more rapid. The question of delay may have some bearing on the best time to administer insulin.

It is evident that if there be a slight delay before the fall with insulin and, in diabetes before the rise in blood sugar after ingestion of glucose, the insulin should be given shortly (not more than half an hour) before the administration of glucose so that the curves may counterbalance one another. Of course these curves show the effect of giving glucose as such in solution by the mouth. The rise in the blood sugar is not so rapid when carbohydrate is given in other forms.

Dr Davies pointed out that in addition to its effect upon blood sugar, or by virtue of that effect, insulin might influence other phenomena which occur in cases of severe diabetes, namely, disturbances of fat metabolism, associated with acidosis, lipæmia, and coma. This subject is a very complex one. A few experiments upon rabbits had been attempted but it was found difficult to obtain consistent results owing to complications such as anæsthesia, shock and hæmorrhage. We were fortunate, however, in having several patients in

whom it was possible to correlate changes in blood sugar and respiratory metabolism with changes in ketone bodies and bicarbonate reserve of the blood. We use the expression "bicarbonate reserve" in the sense of the carbon dioxide combining power of whole blood. A portion of a sample of blood is exposed at body temperature to a known pressure of carbon dioxide (about 40 mm. of mercury) and the amount of carbon dioxide taken up by the blood is estimated. This amount is compared with the assumed normal (that of Haldane's blood) for the same pressure and expressed as a percentage of that normal. The addition of a stronger acid to the blood will displace carbon dioxide and diminish the amount of alkali available for the conveyance of this gas from the tissues to the expired air. If this occurs to more than a fairly limited extent, symptoms of acidosis in the tissues will begin to manifest themselves. The most conspicuous of these symptoms is increased breathing.

The first observation was made on a patient who was not suspected of having a very marked disturbance of bicarbonate reserve. She had from time to time exhibited a certain amount of acetonuria. On this particular day we wished to see what would happen to the blood sugar and also to the blood bicarbonate reserve. At about 9 A.M. the blood sugar was found to be 0·320 per cent., and the bicarbonate reserve 70 per cent. of the normal. Rather more than an hour later the ketone bodies of the blood were further increased, while the bicarbonate reserve and the blood sugar had fallen to 60 and 0·285 per cent. respectively. Ten units of insulin were given at this point. After this the blood sugar continued to fall at a more rapid rate than previously, while the bicarbonate reserve rose rapidly to 90 per cent. of the normal. Coincidently with the rise of bicarbonate reserve there was a fall in the ketone bodies of the blood to an almost insignificant level. The respiratory metabolism showed little change, the only conspicuous event being a fall in the respiratory quotient at the time when the bicarbonate reserve was increasing most rapidly. Lipæmia was present in this case and showed an increase before the administration of the insulin, after which it cleared up rapidly. Another day the same patient was the subject of a similar observation. On this occasion her initial acidosis was not so marked.

She was given 4 units of insulin together with 16 grams of glucose. The results as regards the bicarbonate reserve and ketone bodies of the blood were essentially similar to those of the previous observation.

As a result of these two observations it was considered that it would be of great importance to ascertain whether a severe case of diabetic acidosis would improve if given insulin and glucose alone, without administration of alkali. There had been a case in Professor Meakins' ward some months ago when we were only commencing to use insulin clinically. Not having as yet sufficient confidence in the new remedy we not only gave insulin and glucose but also alkali. In this case the acidosis was of a very severe degree, the blood bicarbonate being only 40 per cent. of the normal. The patient was markedly hyperpnœic, and the case one of the utmost gravity. Insulin, glucose and di-sodium phosphate were given and the bicarbonate reserve rose within a few hours to 75 per cent. of the normal. Two days later it was slightly above the normal but a few days after that it dropped to normal.

As a result of the experience in this case and in the two observations outlined above, it was considered justifiable to attempt to cure any subsequent case of severe acidosis by means of insulin and glucose alone. Two days ago a woman was brought in with hyperpnœa, marked odour of acetone, and mental symptoms strongly suggestive of incipient coma. Examination of her blood showed a bicarbonate reserve only 45 per cent. of the normal. This was indicative of a very severe degree of acidosis. Her blood sugar was 0·39 per cent., while acetone bodies were abundantly present both in the blood and urine. During the subsequent twenty-four hours she received 130 units of insulin and 200 grams of carbohydrate. This was administered at four hourly intervals, blood samples being taken at the same time. Careful observation of the clinical signs and of the bicarbonate reserve showed a marked improvement and justified the withholding of alkali. At the end of the twenty-four hours the patient was free of sugar and the bicarbonate reserve had risen to 89 per cent. of the normal. Also the acetone bodies in the blood and urine had fallen to an insignificant level. The first sample of blood showed marked lipæmia, the second a trace, while in the subsequent samples this had completely disappeared.

Professor Meakins.—A word on the effect of insulin on carbohydrate metabolism in diabetes, demonstrating how its administration increases the retention of carbohydrate.

The effect of a dose of insulin is to produce a decline of the blood sugar, which then remains at a low level for a considerable time. After a glucose meal a diabetic shows a rapid rise in the blood sugar, which continues over many hours. If the same amount of glucose plus insulin were administered, there would be a rapid rise in the blood sugar, and then instead of this continuing to rise, it rapidly returns to normal. It disappears from the blood, probably into the tissues; and this is the great boon which insulin gives to the recipient. We have been able to work out that 1 unit of insulin will, as a rule, look after about 2 grams of carbohydrate.

Synopsis of Five Typical Cases of Diabetes treated with Insulin.

Case I.—Patient aged 44. Came into the Infirmary in an emaciated condition. Long history of diabetes—resisted all forms of treatment. Too ill to venture the starvation procedure and so started on insulin with dietetic regulation. Started on small dose of insulin with a slow decline of blood sugar and glycosuria. Gave him a comparatively free day of diet and increased the insulin. Immediately he was sugar-free, and from then on he remained sugar-free, until he was taking 90 grams of carbohydrate and 200 grams of fat. The insulin was stopped and the diet reduced to 80 grams of carbohydrate. The fasting blood sugar increased and glycosuria returned. The carbohydrate intake was reduced to 70 grams, but the blood sugar increased and glycosuria returning in a few days' time, necessitated a reduction to 60 grams of carbohydrate, at which level he remained well. We decided to start on insulin again; the intake of carbohydrate was increased and he remained practically sugar-free on 105 grams of carbohydrate and 20 units of insulin. That is, an extra 45 grams of carbohydrate, which corresponds to 2 grams per unit of insulin, was added to his diet.

Case II.—A young farmer. Treatment two years ago. He remained sugar-free for two years, but, after pneumonia, developed glycosuria. Returned to hospital for treatment. Adopted the usual methods but could not get his tolerance beyond about 40 grams of carbohydrate. Started insulin, steadily increased carbohydrate and fats until he got over 120 grams of carbohydrate. He got 30 units of insulin a day, which would indicate that the insulin added 80 grams of carbohydrate to his diet. Reduced insulin and immediately his

blood sugar increased and glycosuria appeared. The insulin was increased and the carbohydrate intake left at 110 grams and his urine remains sugar-free and the blood sugar is normal.

Case III.—A female aged 24. In the Infirmary off and on for the last three years with diabetes. Her tolerance for carbohydrate for many weeks was practically nil and her condition was becoming very grave. We started insulin. Her general condition improved although the blood sugar continued above normal. After a low carbohydrate diet for a day the blood sugar fell to normal and the urine became free of sugar. We instituted a gradually increasing diet with insulin, with the result that although we decreased the insulin and increased the diet her blood sugar remained normal; but when no insulin was given the blood sugar increased and the glycosuria returned. She is now taking over 50 grams of carbohydrate and 30 units of insulin, her urine is sugar-free and the blood sugar is normal.

These cases are illustrative of typical cases of moderately severe diabetes which had been under observation for many months and some for years.

Case IV.—A little girl aged 15. She had been under treatment for some four years with a progressive increase in the severity of the disease. The emaciation was extreme and it was hoped to reduce the blood sugar and do away with the glycosuria with insulin. This was done and with 50 units of insulin the blood sugar returned to normal and the patient was able to take a diet containing 75 grams of carbohydrate and 150 grams of fat without glycosuria. Her condition has changed from one of extreme emaciation and weakness to fair nutrition and strength.

Dangers of Insulin.

Case V.—Patient—retired schoolmaster; severe diabetes, diabetic tabes, optic neuritis and alcoholism. It was estimated that his carbohydrate tolerance was about 30 grams per day. He was started on insulin 30 units a day. In thirty-six hours his urine was free of sugar and there was a very distinct improvement in the blood sugar.

About 3 o'clock the next afternoon patient felt a little flushed but he put it down to the fact that he had taken some exercise. He felt slightly sick and very irritable.

3.30 P.M.—Had a short sleep—says he had feeling of apprehension.

3.45 P.M.—Patient awoke in a violent rage, swearing and shouting at another patient in the room for no apparent reason. He was perspiring profusely. Eyes staring. Speech very thick. No twitching. Pulse feeble but not rapid. Whisky 1 oz. in 180 c.c. hot water given. Patient drank this easily and said he felt better though began to feel

shivery. Face looked very congested and veins on temples were very prominent. Pulse improved after the stimulant but patient gradually became more helpless and said he felt "drunk." Saliva dribbling.

4.10 P.M.—Patient cannot hold his head straight (falls to right side)—great difficulty in swallowing, the tea coming down his nose. He ate half an egg and a little tea (usual dose of insulin not given).

4.45 P.M.—Patient is much paler, skin still very moist and cold, cannot speak at all. Unable to swallow.

5.15 P.M.—Patient quite unconscious, incontinence of urine. (Blood taken for sugar = 0.09 per cent.)

Moaning continually with occasional very loud groans (almost a roar). Cannot swallow glucose prepared.

6 P.M.—Intravenous injection glucose grams 45 in 450 c.c. normal saline solution.

6.5 P.M.—Groaning stopped and patient opened his eyes and became very restless.

6.10 P.M.—Consciousness regained; dribbling of saliva stopped. Patient began to speak, saying that his throat was sore and he felt very cold. Glucose 25 grams in 240 c.c. water and lime juice given by mouth and swallowed easily.

6.30 P.M.—In spite of hot bottles and blankets patient still complains of cold (bed moved into big ward).

7 P.M.—Patient sitting up in bed feeling well and hungry and much warmer. He remembers nothing from the time when his tea was brought in at 4 P.M. until he found himself in big ward at 6.30 P.M. He remembers the onset of the attack very distinctly and says he knows he lost all control and was shouting and swearing when the attack came on. Says the irritability seemed to "come over him in waves," leaving him with a feeling of nausea.

Got about 70 to 80 grams carbohydrate. After this he was kept upon insulin with a very generous diet. But he was apt to show symptoms of hypoglycæmia in the late afternoon in spite of the fact that there was a high fasting blood sugar and glycosuria between 4 A.M. and 11 A.M. Cases of this type are frequently met with. In them hypoglycæmic symptoms frequently develop in spite of there being glycosuria during part of the day. Through this treatment the tabetic symptoms are rapidly disappearing, the optic neuritis has disappeared and the alcoholism is cured.

This case illustrates the danger of insulin.

Coma.—Dr Davies has referred to the question of acidosis. Acidosis is always an accompaniment of coma. Why patients develop coma has intrigued physicians for centuries but it would seem that now a great deal of new light would be shed upon the question. Coma seems to appear as a result

from tissue starvation. The tissues are bathed in food stuffs but apparently cannot use them. The effect of cyanide poisoning on tissue oxidation might be cited as an analogous process. It was with a view to attempting to elucidate this condition that some of our observations were undertaken.

The following is the synopsis of the case of a young woman who came in to the Infirmary and next day developed coma. No treatment had been initiated. There was a very high blood sugar and we treated her with insulin, alkalis (di-sodium phosphate), and glucose. We consider that the most important of these are glucose and insulin. The alkali goes to neutralise ketone bodies present while the insulin and carbohydrate allow the tissues to acquire what they are lacking and promotes the more complete combustion of fats and fatty acids. This patient got 80 units of insulin and 462 grams of carbohydrate in a day, the greater part of which was retained although at one time the blood sugar increased to 1 per cent. Within a day she was quite conscious, and all signs of acidosis had disappeared. She continued to have hallucinations for about ten days, which were apparently a a sequel to the damage wrought by the cause of the coma.

Case VI.—A female aged 38, who was admitted with a severe acidosis and semi-consciousness. She was given 190 grams of carbohydrate and 100 units of insulin in sixteen hours, with a preliminary but comparatively small rise in blood sugar and subsequent continuous fall during the next twenty hours when it was just over 100 mgm. per cent. and the urine was free of sugar. Within twelve hours all signs of acidosis and coma had disappeared and it was necessary to increase the carbohydrate intake to prevent hypoglycæmia. This case demonstrates the great value of insulin and carbohydrate combined in the treatment of diabetic coma.

Insulin in itself is not a cure for diabetes, it merely gives the patient an increased facility for using carbohydrate, and it must be combined with the proper control of the diet. The taking of insulin without such control will probably lead to disastrous results. We have as yet no definite evidence that insulin increases the tolerance for carbohydrate consumption, but I think we have evidence to show that insulin plus dietetic treatment may lead to such an increase. In addition insulin affords us a means of overcoming and circumventing the dangerous emergencies of diabetes.

The President, Sir Robert Philip, in thanking the various speakers for the lucid presentation of the subject, dwelt on its importance both from the physiological and from the therapeutic point of view. Only a few months ago the subject of diabetes had been ably reviewed before the Society by their late friend Dr Harry Rainy. On that occasion a strain of pessimism coloured the discussion. That had been replaced to-night by a remarkable note of optimism. The darker incidents attaching to diabetes had been especially lightened by the researches of Banting and Macleod. To-night valuable corroborative evidence had been submitted. The optimism must not be carried too far. There were obviously limits to the efficacy of insulin and attendant risks might yet have to be considered. None the less, those researches, bearing as they did on one of the gravest emergencies in medical practice, fell to be included among the most noteworthy additions to therapeutics within recent times.

Discussion.

Dr John Cowan gave a short summary of the results which were obtained by the team working at the Glasgow Royal Infirmary. These had been satisfactory. Insulin could not be regarded so far as a cure but it might be of great service in emergency.

Dr Chalmers Watson complimented Professor Meakins and his collaborateurs on their excellent series of papers. In addition to the admirable statement of their results so clearly presented, the Profession had recently the advantage of seeing in print a summary of the results of treatment by insulin in all the various centres promoted by the Medical Research Council, in all fifty cases having been treated, including seven cases of diabetic coma. The impression conveyed from the perusal of this was that the recent discovery of insulin was a much more important advance from the point of view of physiology than from the point of view of practical medicine. Time and experience might, however, show that insulin was of more important therapeutic value than was so far suggested by the initial results from its use. It was interesting to observe from these initial statements of the Research Council that the conclusion had been arrived at that there was no definite relation between the amount of blood sugar and the presence of coma. Keeping this in view, it was interesting to note that Dr Lambie laid stress on the amount of blood sugar in the rabbit as a method of standardising the dose of insulin. From numerous observations on blood sugar in well-marked cases of diabetes of many years'

standing, the speaker had been impressed by the limited value of blood sugar estimations, and he was inclined to the belief that too much importance was at present attached to blood sugar as a guide to treatment. Dr Lambie had referred to the individual variability of animals as regards their response to the injection of insulin, and also, in the latter part of his paper, to the great difference in susceptibility of animals. This emphasised the need for special caution in drawing any deductions applicable to the clinical conditions in man. Any deficiency of insulin presumably depended upon a local lesion of the pancreas, and was the result of some disturbances of that gland. It seemed to the speaker important to attach more importance than was usually done to the investigation of ætiological factors which might be *the cause* of that disturbance of nutrition. One of the most important lines of investigation was the study of local infections. There is some reason for thinking that latent focal infections of a kind not generally recognised, because not adequately looked for, might, in many cases, be the determining factor in inducing the disturbance of the function of the gland.

SPECIAL CLINICAL MEETING.*

Mr J. J. M. Shaw showed three cases illustrating the persistence of **salivary fistulæ** and their methods of treatment.

(1) J. M., æt. 24, was wounded on 25th August 1918, by a bullet which entered immediately below the lobule of the left ear and made exit in the mid-line of the neck posteriorly. A fistula of the parotid gland developed. In August 1920 the epithelialised lining of the track was excised and the wound sutured over, but healing did not take place and the amount of the salivary discharge was greater after operation than before. In May 1921 the track was cauterised and sutured. It remained dry for two days only, but the flow was slightly diminished in quantity.

He was admitted to Craigleith Hospital in March 1923 and on the 12th of that month, after the insertion of a strand of silkworm gut along the track, half an inch of the fistulous channel was excised. The cautery was then applied to the stump, and after complete excision of the funnel of scar tissue which had surrounded the fistula the wound was closed by deep catgut and skin sutures. It has remained completely dry since this operation and may, after the lapse of these two months, be regarded as cured.

(2) F. M., æt. 45, was wounded on 10th March 1915 through the right cheek, with fracture of the hard palate and exit on the left side. The parotid duct was torn in the pre-masseteric region and a fistula developed.

In April 1919 an attempt was apparently made to prolong the channel forwards by making two parallel incisions, one-fourth of an inch apart, in the normal line of the duct, thus leaving a strip of skin immediately in front of and continuous with the fistulous opening. The strip of skin was then led into the mouth at its anterior end and, by suture of the free skin edges of the cheek, the mouth of the fistula and the narrow strip of skin were buried in the cheek. This operation failed as one would expect from the employment of a hair-bearing strip of skin, and sebaceous and purulent discharges were added to the pre-existing salivary flow on to the cheek. In the four succeeding years four attempts were made to reintroduce this track into the mouth and on one occasion a large acute abscess called for incision.

When admitted to Craigleith Hospital in March of this year, the ends of several long hairs protruded from the orifice on the cheek, and the line of the track was thickened, inflamed and tender. The patient was told that the first stage in his treatment would be the elimination of this hair-bearing septic track and that the cure of the fistula at this

* Held 16th May 1923.

operation would be improbable. Free excision of the track was affected by open dissection and a considerable amount of the surrounding scar tissue removed. When this was completed the stump of the duct was drawn, under moderate tension, through a stab incision into the mouth and stitched to the mucous membrane with catgut. The skin edges were approximated by suture.

For a week there was a slight sero-purulent discharge from the cheek surface, but there has been no visible escape of saliva, and his dressings have at no time been positive to the ferric chloride test for saliva. The affected area is still slightly tender and reddened; until these signs disappear and remain absent for a considerable time the case cannot be considered to be cured, but there is reason to hope that further operation may be unnecessary.

(3) J. F., æt. 53, was wounded in the left cheek in September 1916. His condition is not quite accurately described as a salivary fistula, the wound being in the naso-labial fold and the course running from cheek to mouth anterior to the buccal orifice of Stenson's duct. In addition to the discharge of saliva the patient was therefore troubled with the escape of any fluid which he took into his mouth and, on filling his mouth with tobacco smoke, could emit a fine jet of smoke through the fistula.

For the first three months following the wound the discharge was intermittent, but thereafter the fistula remained open. The track was excised in February 1922. It remained healed for two months, but again broke down, and the patient was admitted to Craigleith Hospital in March of this year. On 19th March, through an incision in the naso-labial fold a large block of scar tissue was excised with the fistula in its centre, and healthy tissues opposed to one another. The wound has been completely healed since that time and should remain so.

Emphasis was laid upon the need for the free removal of scar tissue in these cases in addition to the epithelialised track which it encloses. Scar tissue is easily digested by proteolytic enzymes whether of micro-organisms or of the tissue extracts or body fluids on account of its avascularity and consequent poverty in the anti-enzymes of the blood serum of healthy tissues. Saliva, in addition to its main function, has a mild proteolytic action and, although far inferior in strength to specific protein splitting agents such as are produced by the pancreas, is nevertheless described by Wells as being experimentally "quite active" in this respect. It is probable that this chemical action is of some importance in explaining the persistence and tendency to recurrence of salivary fistulæ.

Mr Wilkie showed—(1) a case of **pharyngeal diverticulum**. Male, æt. 54, acute difficulty of swallowing of six weeks' duration, latterly unable to swallow fluids, attempts to do so caused much spluttering, and inspiration of fluid had set up marked bronchitis with

very profuse expectoration. X-ray showed diverticulum descending behind œsophagus, almost directly in mid-line, if anything, bulging to the right side. Operation two weeks previously under local anæsthesia, diverticulum freed and brought to the surface on the right side of the neck with the object of two-stage resection. Since first operation patient had been entirely relieved of all difficulty in swallowing and the bronchitis had rapidly cleared up. It was a question, therefore, whether anything further should be done in view of the striking immediate result from the diverticulopexy.

(2) A case of **carcinoma of the rectum**. Male, æt. 65. Six months after radical operation by the following procedure which is devised to combat sepsis, hæmorrhage and shock:—preliminary colostomy, interval of two and a half weeks during which time bowel washed out daily and three doses of a mixed streptococcus and B. coli vaccine given. The night before the second operation 8 c.c. of 2 per cent. nucleinic acid given subcutaneously to produce leucocytosis, omnopon scopolamine twilight sleep, spinal anæsthesia, 6 c.c. 10 per cent. stovaine. Patient placed on his face in inverted V position, perineal excision after removing coccyx. Operation unattended by any hæmorrhage or shock.

Sir David Wallace showed two cases of **nephrectomy for pyonephrosis**. (1) Mrs P. A., æt. 33, transferred from Professor Gulland's ward. Severe pain in left lumbar region two years ago, which ceased in two days and was associated with no urinary symptoms. Since then attacks of pain have been frequent. During last six months micturition frequent, and sometimes blood in urine. X-ray negative. Many organisms but no tubercle bacilli in urine. Kidney easily palpable and tender. Chromo-cystoscopy: bladder healthy, right kidney secreting normally, nothing from left kidney. Operation 11.4.23, left kidney, pyonephrosis. Nephrectomy.

(2) Mrs S. A., æt. 42, transferred from Dr Fordyce's ward. Severe pain in left lumbar region nine months ago, fever, frequency of micturition both by day and night. No blood in urine, but some deposit. Recovered from attack. Four months ago recurrence of symptoms. Kidneys not palpable. Urine containing pus and many organisms, but no tubercle bacilli. Chromo-cystoscopy: bladder healthy, right kidney secreting normally, nothing from left kidney. Operation 20.4.23, left kidney, pyonephrosis with calculi. Nephrectomy.

Mr W. J. Stuart showed a case of **ureteral transplantation**. Female. Extensive laceration of the anterior vaginal wall and base of bladder occurred at her first confinement in July 1922, and the urethra was torn away. Constant dribbling of urine, with intense skin irritation, patient being entirely confined to bed. Local repair was impossible. Ureteral transplantation into the pelvic colon was performed trans-

peritoneally in December 1922. Patient now evacuates urine by the rectum, but at intervals of four hours, so that she is able to do her work and lead an almost normal life with little inconvenience. Her general health is excellent.

Mr J. W. Struthers showed—(1) a case of **hyperostosis of the frontal bone** probably secondary to an endothelioma of the dura mater. The patient was a young man æt. 22, who had suffered for some months from a painless swelling on his forehead. The swelling took the form of a flattish elevation about the middle of the forehead, measuring two and a quarter inches horizontally and one and three-quarter inches vertically. Towards its left lower corner there was a small conical elevation raised above the level of the rest of the swelling. The swelling was of bony hardness and shelved off gradually into the surrounding bone. There was no pain or tenderness and no other symptoms were complained of. A radiograph showed a diffuse thickening of the bone in the area occupied by the swelling with some erosion on the inner aspect. The Wassermann reaction was negative on two occasions and a course of anti-syphilitic treatment had no influence on the swelling.

The absence of any trace of inflammatory reaction in the swelling and scalp and its failure to respond to anti-syphilitic treatment seemed to indicate that the swelling was neoplastic in character. Its site and general characters corresponded closely with the bony outgrowths found in association with endothelioma of the dura mater and the provisional diagnosis accordingly was "hyperostosis secondary to dural endothelioma." The result of the exploratory operation would be related at a later date.

(2) A man æt. 25 who had suffered from attacks of **biliary colic** for two and a half years. At the operation his gall bladder was found thickened and tightly packed with gall stones and was removed. The case was of interest in so far as the condition is uncommon in young males of good physique and because the patient was the fourth member of his family to be operated on for gall stones, one sister and two brothers having already been operated on for cholelithiasis.

Mr Henry Wade and *Mr J. J. M. Shaw* showed a case of **chronic empyema** following tuberculous disease of pleura, treated by extensive thoracoplasty. J. C., æt. 23, developed left-sided pneumonia in August 1920, shortly after return from long period of exposure and hardship on board a destroyer off North Coast of Russia, during which his health is stated to have deteriorated. Slow recovery from pneumonia (three months in bed). A fortnight after being allowed up, left pleural cavity was tapped and fluid of tuberculous type withdrawn (at Plymouth Naval Hospital). In January 1921, 2 inches of 10th rib resected and long drainage tube inserted. Continuous tube drainage with steady loss of weight and strength until admission to Craigleith Hospital in July 1922.

On admission. General condition poor, drainage tube *in situ* with considerable discharge. Left lung collapsed with massive thickening of pleura and cavity extending from level of discharging sinus at 10th rib to apex. Heart pushed over to right and slight secondary scoliosis.

September 1922. Thoracotomy by further rib resection; free drainage established. December 1922. General condition much improved by last operation but cavity undiminished in size.

Operation: large U-shaped flap turned upwards, centred at posterior axillary line and including scapula. Resections of large portions (5 to 6 inches) of 5th to 10th ribs with full exposure of cavity which reached pleural dome. Extensive excision of greatly thickened pleura. Flap of soft parts folded upwards and cavity left exposed. Operation followed by further marked improvement in general condition.

March 1923. First stage in repair of cavity. Scapula exposed by extension of posterior limb of U incision. Muscles covering ventral and dorsal aspects of lower half of body of scapula detached subperiosteally from below upwards. Lower half of scapula overhanging cavity removed by section parallel to spine. Granulation tissue at apex of cavity scraped with sharp spoon. Subscapularis muscle folded upwards to fill upper part of cavity; infraspinatus fell naturally into central portion of cavity and there sutured. Shelf of healed granulation tissue corresponding to original sinus left to ensure drainage. Lower 2 inches of skin flap left resting unstitched upon this shelf.

April 30th, 1923. Shelf of granulation tissue excised and lowest portion of flap loosely stitched into position.

Weight before pneumonia, 10st. 3 lbs.; June 1922, 8st. 6 lbs.; April 1923, 8st. $10\frac{3}{4}$ lbs.

Family history, nil to note. F. and M. alive, three brothers and two sisters alive and healthy. Two sisters died in infancy.

Mr Wade showed two cases illustrating **plastic surgery for cranial defect** following gunshot wound of the skull. (1) The first case was J. R., æt. 32, who was wounded on 4th March 1915 by a rifle bullet penetrating the skull. Since that day he has been in a state of more or less constant ill-health, subject to fits and suffering from periods of extreme mental depression. Latterly suicidal tendencies developed and he was treated for a self-inflicted wound. On recovering from this the operation was performed, the cranial defect being filled in by a bone graft obtained from the adjacent outer table of the skull. This operation was carried out on 30th January 1923. His convalescence was uneventful and his general health is now excellent.

(2) The other case was one about to be operated on. His history was very similar as regards fits and mental depression. Mr Wade has now operated on ten cases of this nature, all of which have given most satisfactory immediate results. He mentioned, however, that it was too soon yet to make a statement as regards the final consequences

of treatment, but the result obtained to date was highly satisfactory in every way.

Mr Pirie Watson showed—(1) a case of **traumatic thrombosis of popliteal artery.** A. H., boy, æt. 11, had climbed to the top of a stone gateway 9 feet high, ornamented on top by a spherical stone 15 inches in diameter. When he grasped this stone ball it became displaced, and he and it fell to the ground together. The ball, which weighed ¾ cwt., struck his left leg, producing an oblique fracture below the head of the tibia, and a small puncture wound behind the knee-joint. A hæmatoma rapidly formed in the calf and popliteal space, and the foot and leg became dusky red, cold and insensitive.

Operation within three hours; blood-clot cleared out; no bleeding vessels found. Popliteus muscle, both heads of gastrocnemius, posterior capsule of knee-joint and genicular branches of popliteal artery and vein ruptured, *i.e.* rupture of all structures in popliteal space other than main vessels and nerves, as if damage produced by sudden forcible hyperextension of knee-joint. The popliteal artery was bruised but pulsating feebly. Wound closed and drained. For some days the vitality of the limb hung in the balance, but on the sixth gangrene of foot and lower two-thirds of leg was evident. Miller's amputation through the knee-joint was performed.

The popliteal artery was found completely thrombosed. The collateral circulation, always feeble for the popliteal artery, was rendered inadequate in this case by the rupture of the genicular branches.

(2) A case of **osteochondritis deformans juvenilis** affecting left hip-joint. J. S., boy, æt. 8. Limp first noticed two years ago. No pain but limb easily tired. Can run, jump and hop on toes without discomfort. Abduction markedly restricted, internal and external rotation impaired. Thigh slightly flexed and adducted, gluteal fold marked, pelvis tilted upwards on affected side; slight lumbar scoliosis; convexity to right; apparent but no real shortening; half-inch wasting in thigh, no wasting in calf. Boy is healthy and well built, one of a family of four, all alive and well. No illnesses except those of childhood; fell downstairs when aged 2, otherwise no accident of note. Early tuberculosis disease at first suspected, but radiogram showed changes associated with osteochondritis deformans juvenilis:—flattening and segmentation of epiphysis of head of femur; rarefaction, shortening and broadening of neck of femur; crenation of acetabulum.

Treatment—Massage; elimination of body weight by Thomas's hip splint, patten, and crutches for almost one year. No obvious change in condition. Splint now discarded and patient to be kept under observation.

Dr Robert A. Fleming showed three cases of **lethargic encephalitis**—(1) V. F., female, æt. 17, admitted to Ward 24, 20th March 1923. Complaining of headache, drowsiness and diplopia. Onset of illness was a

week previously. The headache was mainly frontal and shooting pains were complained of affecting left side of face and left shoulder. Pyrexia running up to 104° F. lasted for ten days and was accompanied by extreme drowsiness ; often patient could not be roused without much stimulation. Voice was monotonous, with pitch altered from the normal. When roused, marked ptosis was noted, and this continued long after recovery and was present even after discharge from hospital. During the earlier pyrexial period there were hallucinations with mild delirium especially at night. When very drowsy catalepsy was marked. Diplopia passed off in a fortnight. Slight nystagmus was observed but became less obvious after four weeks in hospital. Patient was treated by repeated lumbar puncture and benefit followed each operation. Fluid contained a slight excess of lymphocytes, but no organisms were obtained by culture. A fixation abscess was produced and resulted in a leucocytosis of 16,000. Leucocyte count fell very gradually, even on discharge on 7th May it was over 11,000. Hexamine was administered in full doses. The patient made a satisfactory recovery.

(2) A. B., schoolgirl, æt. 13, was admitted to Ward 24 on 13th March 1923. She was absolutely unconscious on admission. The onset dated from three weeks before entering the ward. She was very thin, and the chief feature of the case was the rapid development of rigidity with head retraction, curvature of the spine and contracture of arms and legs. There was marked squint from time to time, but although the cornea was sensitive to touch the girl could not be roused or made to do anything she was asked. There was marked catalepsy when it was possible to extend the limbs. Incontinence of urine and fæces was present almost from the outset. Notwithstanding the deep stupor liquid food was easily administered. Emaciation became more marked. Pyrexia was never very pronounced. At first about 100° F. it gradually fell to normal. She was treated by repeated lumbar puncture, fixation abscess and hexamine. The cerebrospinal fluid was at first under slight pressure. There was an excess of lymphocytes though not marked. Attempts at culture failed. The girl improved in so far that the contracture is not so marked and the limbs can be extended, but she still remains comatose and is excessively emaciated.

(3) T. H., boy, æt. 10, admitted to Ward 23 on 27th March 1923. Onset of illness was 24th January. He complained before admission of severe pains shifting from place to place and accompanied by rapid myoclonic contractions of limbs and trunk muscles. These twitching movements were also seen when he was sleeping. He had marked ptosis but no diplopia was complained of. There were marked hallucinations, such as that the family cat was just about to fly at him and that he was just about to "fly up" himself. The difficulty experienced with this patient was extreme restlessness and terror at night and inability to keep awake all day.

He is gradually improving with general treatment and suitable sedatives given to induce sleep at night—paraldehyde being of special value. The choreic jerkings are less marked and the ptosis is passing off. He had little pyrexia probably because the stage when temperature was present preceded admission to hospital. Neither lumbar puncture nor fixation abscess were resorted to in this case.

Dr Charles M'Neil showed two cases of myoclonic type of **epidemic encephalitis**—(*a*) A. P., æt. 11 years. Onset of illness on 1.2.23, with severe and shifting peripheral pains, followed by rapid myoclonic contractions of trunk and limbs. Other features were transient hiccough, cerebral excitement and insomnia, retention of urine and incontinence of fæces. Slow steady improvement.

(2) W. G., æt. 11½ years. Onset on 9.3.23. with severe and shifting peripheral pains followed by myoclonic contractions of arms, feet, and upper abdomen. Other features were diplopia, insomnia and mild excitement, a series of convulsions, and retention of urine. General steady progress except for persistent slight myoclonus of intercostal muscles.

Prof. Edwin Bramwell demonstrated two cases of **lethargic encephalitis**, a peculiar feature of which consisted in the prominence of subjective sensory symptoms.

Professor J. C. Meakins showed a case of **hyperthyroidism**. I. I., girl, æt. 16. For two years had complained of swelling of the neck, and shortness of breath for the past five months. No exophthalmos or nervous symptoms. Menstruation began shortly after enlargement of the neck and has been irregular.

Basal metabolism on 26.5.21. . . . – 10 per cent.
„ „ „ 31.5.21. . . . – 16 „

Cod-liver oil and iodine were given, and the patient sent home to return for observation.

29.8.21.—Size of neck unchanged. Iodine increased.

8.3.22.—Size of neck 2 cm. smaller. Basal metabolism plus 14 per cent.

17.7.22.—Patient readmitted to hospital with marked tachycardia, exophthalmos, continued enlargement of thyroid, and fine tremor. Basal metabolism plus 55 per cent. Rest in bed with withdrawal of the iodine showed a progressive improvement in the condition.

26.7.22.—Basal metabolism, plus 22 per cent.
7.8.22 „ „ „ 20 „
18.8.22 „ „ „ 13 „
1.9.22 „ „ „ 20 „
3.11.22 „ „ „ 2 „

The symptoms of hyperthyroidism appeared during a prolonged period of iodine administration.

Special Clinical Meeting

Professor J. C. Meakins and *Sir Harold Stiles* showed E. S., female, æt. 45. Complaint: Swelling of the neck and lack of energy. Duration five years. Chief complaints were progressive tiredness, lack of energy, perspiration, easily fatigued, progressive nervousness, loss of weight. Moderate exophthalmos and tremor. B.M.R. plus 40 per cent. Pulse-rate 100. Blood-pressure 165/80. Diagnosis — **toxic adenoma of the thyroid.**

Operation: Removal of the thyroid. Microscopic examination shows numerous small adenomata.

Progress: Pronounced improvement of all symptoms. Within ten weeks basal metabolism returned to normal, pulse to 78, blood-pressure 120/80.

Present condition: Continuation of improvement.

Dr G. D. Mathewson showed Mrs M., æt. 48. Admitted Leith Hospital, 1.10.20. **Exophthalmic goitre,** auricular fibrillation, enlargement of liver and spleen. Wassermann negative. Progressive failure of strength with œdema of legs and trunk, ascites and right pleural effusion. Complete recovery under mercury and iodide, with subsequent obesity reduced by thyroid treatment.

Dr W. T. Ritchie showed four cases of **auricular fibrillation.**

1. *Auricular fibrillation abolished by quinidine.*

Tramway labourer, æt. 20. Chorea at 12; aortic incompetence for probably four years; fibrillation for unknown period. Normal cardiac rhythm restored on 15th January, after 1.8 g. of quinidine in three days, and maintained for six weeks while patient taking 0.2 g. twice daily. Readmitted 21st March, fibrillating; spontaneous restoration of normal rhythm one month later.

2. *Auricular fibrillation persisting despite quinidine.*

(*a*) Blacksmith, æt. 42. Rheumatic fever at 16; previous chorea. No history of V.D. Wassermann negative; aortic incompetence and fibrillation of unknown duration. Fibrillation persists despite 59.6 g. quinidine in thirty-six days, and later 26.6 g. in fifteen days.

(*b*) Paperworker, æt. 37. Acute rheumatism with pericarditis at 15; mitral stenosis and incompetence; fibrillation of unknown duration. First quinidine course, March 1922, with maximal daily dose of 0.4 g. six-hourly for seven days. Second course, December 1922, 20.4 g. in eleven days. Third course, April 1923, 11.0 g. in ten days.

3. *Auricular fibrillation with Adams-Stokes syndrome.*

Engine-keeper, æt. 34. Mitral stenosis and incompetence; fibrillation of unknown duration with partial auriculo-ventricular block. Admitted for fourth attack of acute rheumatism. When convalescing, given 1.4 g. of quinidine; two Adams-Stokes seizures, during which he was thought to be dead. Improved by atropine.

THE MUSCULATURE OF THE AORTA AND OF THE CARDIAC VALVES, ANATOMICALLY, PHYSIOLOGICALLY, AND CLINICALLY CONSIDERED.*

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ALTHOUGH in every field of observation we are liable to err, I am not, I think, propounding a heresy when I state that, on the whole, the experiments and conclusions of the physiologist are more liable to revision than the observations of the anatomist. Both are descriptive and interpretive, but the study of action and function is, perhaps, more difficult than that of structure and structural change.

Anatomical study may, nevertheless, indicate both function and the wider conditions of environment. The more intimate relations of blood-supply and innervation may also be appreciable from anatomical observation, and I would even go further and maintain that there are situations in which, in the differences between conclusions as to function drawn by the anatomist and the physiologist respectively, the former may, with some confidence, expect an ultimate decision in favour of the correctness of his views. *Sine anatomia trunca et debilis esset medicina* (Celsus). It is from the point of view of the clinician—the student of anatomy and physiology, applied at the bedside, that I approach the consideration of the particular subject of my present communication.

There is a considerable literature on the development, blood-supply, mechanism, and action of the valves of the heart, but the subject has not often been examined with the minuteness and detail which it merits. Our text-books in dealing with it, in some instances, consider the subject with a brevity and superficiality, which can only be justified on the assumption that the matter in question is unimportant. To this there are of course exceptions, but, even in these cases, it is not treated so fully as the clinician would desire. For example, one searches in vain, as a rule, among records consulted by more recent writers on the subject for the "Observations on

* Read 6th June 1923.

the Structure and Connections of the Valves of the Human Heart," by W. S. Savory, then Tutor to St Bartholomew's Hospital, and contributed by him in 1851 to the *Proceedings of the Royal Society*, and to the *Lancet* in 1852. But in that excellent paper, the character of the work in which was prophetic of his future distinction and practical sagacity, Savory gave what was, till then, the best account of his subject; and it is on many points correct, with little modification now, as one would expect in the case of accurate anatomical observation.

The technique of microscopical investigation has, however, in some respects improved since he wrote, and modern staining methods in a rising scale of animals afford a more satisfactory view of both the structure and indicated function of the musculature and connections of the conditions in question, than can otherwise be obtained.

In investigating the matter, I have done so in the fish, the bird, the mammal, and to a certain extent in man; but the size of the human heart, and the necessary precedence of death for a considerable period before examination is possible, render the section and staining of material more difficult in him.

Savory, summarising his work, states (*loc. cit.*) that he had attempted to explain "the real connection that exists between the auricles and ventricles, and their relation to the fibrous rings; the formation of the grooves in which the coronary vessels lie; the nature and mode of formation of the tendinous festooned rings surrounding the arterial orifices; the exact connection existing between the semi-lunar valves and the upper border of the ventricles upon which a portion of the valves rests, and by which they are supported; the different tissues entering into the formation of the arterial and auriculo-ventricular orifice, and the construction of the anterior mitral valve."

In his "real connection" between the auricles and ventricles he did not, of course, show muscular continuity between the chambers, although some of his illustrations which are diagrammatic appear to do so, but the passage of auricular muscle into the valve flaps, especially into the aortic cusp of the mitral valve, and the relation of the auricle to the aorta itself. He also did not concern himself with the character and relations of the auricular musculature, which plays so important a part in the cardiac mechanism of the circulation through the heart, at the inlets to that organ. While his observations were

made chiefly on man, he also studied the question in the larger quadrupeds, and described the relations of the so-called "cardiac bone" in those animals in which these supporting bodies are to be found. It will thus be seen that he considered the subject from an anatomical standpoint very fully, and it is because, notwithstanding this fact, his work is now rarely referred to, that I have recalled it at some length.

The study of the auricle, ventricle, and bulbus arteriosus of the fish, as Sir Arthur Keith has well shown, demonstrates the principle of the reception and propulsion of the blood most simply, and likewise indicates the high pressure conditions to which the exposed gills and, in the case of the selachians, the whole body of the fish is submitted, in the heavy medium inhabited. The powerful musculature, dense fibrous structures and thick vessels of the avian heart and vascular system, which adapt the bird to sustained movement at various altitudes, and which appear to be retained even by those members of the family which have become apteric, is instructive and not without practical interest, as indicating the principles of adaptation by man to circumstances, by cardio-vascular changes of an analogous nature, well known to the clinician. But it will on the whole be most convenient for my present purpose to examine the matter in the mammal, and to refer only incidentally to illustrative points in pre-mammalian creatures. I shall consider the matter under the following heads:—(1) The auriculo-venous cardiac entrances; (2) The auriculo-ventricular valvular mechanism; (3) The ventriculo-arterial exits.

I. The Auriculo-Venous Cardiac Entrances and the Auricle.

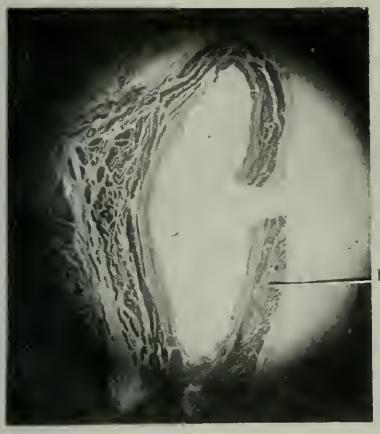
We may commence with the entrance of the superior vena cava into the right auricle. Sections of this segment in the pig, taken as representative mammal, show that the entrance of the superior vena cava into the right auricle is anatomically distinct from the auricle and bridged by the sino-auricular node, although in some sections the venous and cardiac muscles are seen to be in very close connection. The auricular end of the vein has, moreover, a powerful muscular development, and, connected by the node and the nervous system controlling the latter with the auricle, may even be regarded as a para-auricular structure, using that qualifying term as one

does the expressions para-thyroid and para-sympathetic. In other words, the lower end of the superior vena cava is, in function, a detached or supplementary portion of the auricle.

The sinus venosus is regarded by embryologists as merged into the commencement of the auricle and the sino-auricular node in the mammal. But the relations of the auricle to the superior vena cava very strikingly resemble those existing between the coronary sinus (which is regarded as a survival of the left horn of the sinus venosus) and the auricle. If morphologically not representative of the sinus venosus but of the right duct of Cuvier (Keith, *Embryology*), the auricular end of the superior vena cava plays the part anatomically and physiologically of that structure in the earlier heart, and its sphincteric occlusion necessarily precedes the larger auricular systole. Contraction in the cardiac cycle may be observed to commence here and spread to the auricle. This has later been denied, but I think on insufficient grounds. The contraction of this cavo-auricular segment, besides starting the series of cardiac events (granted that it be on the incentive of the fully innervated sino-auricular node that it does so), is also sphincteric to reflux from the auricle into the superior vena cava. If this be questioned, dubiety may be set at rest by an examination of the entrance of the sinus venosus into the auricle of the fish, where a powerful circular muscle or constrictor develops, to prevent reflux from the auricle.

The importance of the coronary sinus has not always been fully appreciated. Prevented by powerful valves from impeding the coronary venous circulation during its contraction, and protected by the Thebesian valve and the narrowing of its orifice during auricular systole, it may be regarded as the venous heart of the coronary system. Surrounded in some measure by auricular muscle, but not wholly, its contraction is, nevertheless, like that of the entrance of the superior vena cava into the latter, if not prior to, yet in the earliest phase of auricular systole, and thus helps to empty the coronary venous system. These relations of the coronary sinus are well shown in cases in which the right auricle is hypertrophied (Fig. 1).

The conditions of the inferior caval entrance are not quite the same as those of the superior cava and those of the coronary sinus. The effective closure of this entrance, provided though it be with a once powerful valve (the Eustachian), is



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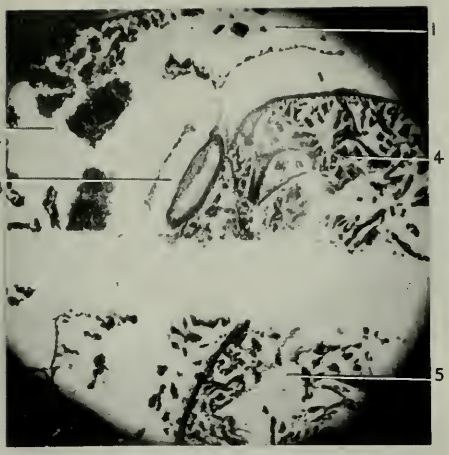

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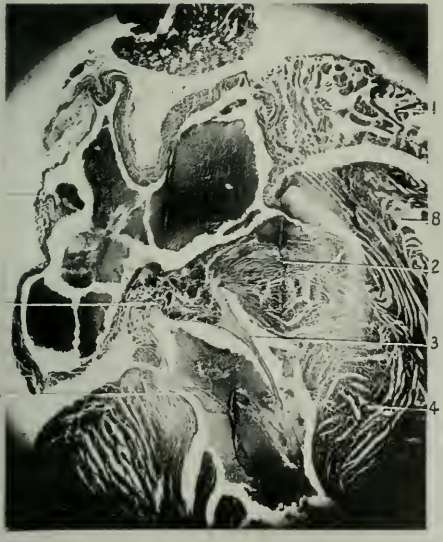

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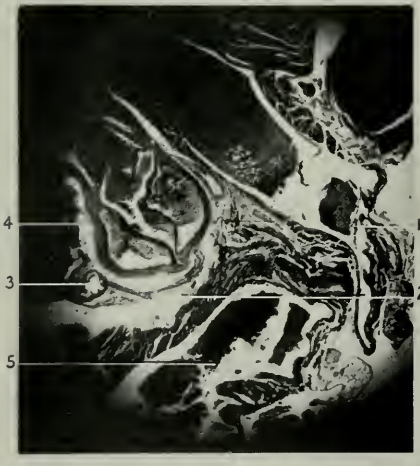

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FIG. 1.—Man. 1. Coronary sinus, showing its muscular character.

FIG. 2.—Minnow. 1. Sinus venosus. 2. Auricle. 3. Auricular sphincter of the auriculo-ventricular orifice. 4 and 5. Ventricle.

FIG. 3.—Mouse. 1. Left auricular appendix. 2. Basic ventricular cusp-tightener. 3. Mitral cusp. 4. Left ventricle. 5. Mitral cusp. 6. Auricular mitral sphincter. 7. Left auricle. 8. Conus arteriosus.

FIG. 4.—Mouse. 1. Posterior aortic cusp. 2. Tendon of rotator basis aortae. 3. Left coronary artery. 4. Left anterior aortic cusp. 5. Left auricle.

aided by the contraction of auricular muscle during its systole, in which condition the Eustachian valve probably acts more efficiently than its dimensions in the flaccid auricle suggest.

This mechanism likewise applies to the pulmonary venous entrances into the left auricle. Here, guarding valves are absent, but by the contraction of the chamber itself, in an early phase of auricular systole, at the orifices of these entrances the pulmonary veins are secured against reflux, and even deeper in the veins, at their smaller bifurcations, the muscular structure of the vessels indicates the mechanism which prevents regurgitation into the venous system in question. Transverse sections of the heart of a mouse stained by the van Gieson method show this point.

Contraction, then, commencing at the superior cavo-auricular junction traverses or is taken up by the auricles which empty themselves into the ventricles, the final act of auricular systole being in the cis-ventricular, that is, the auricular portion of the auriculo-ventricular segment. Here, a happy section of the auricle in the fish may show a complete muscular sphincter at the mouth of the auricular purse so to speak (Minnow, Fig. 2). Nor is this observable only in the fish but also at the left auriculo-ventricular orifice in the bird, and at both auriculo-ventricular orifices in the mammal. On the right side in the bird, as we know, a very perfect and completely muscular mechanism plays the part of the tricuspid valve, and this mechanism, be it noted, is at the commencement of the ventricle, a part of that chamber, and apparently also of the right auricle. The physiological import of this fact is interesting. It indicates, I suggest, a localisation of muscular action pointing to a local control which is not at present conceded by the physiologist, but necessitated by the conditions of the avian pulmonic circulation. On the right side in the mammal, while the complete control of the outer auriculo-ventricular valvulature by the auricle may readily be shown, the attachment of a portion of the internal septal cusp of the tricuspid valve to the auricular end of the ventricle shows that this portion of the valve is not so completely controlled by the auricle during ventricular systole, as are the anterior and posterior segments in the normally developed heart.

The importance of sufficient atrio-ventricular closure by muscle, and support by normally developed fibrous structures in maintaining the circulation through the heart is well shown

when, from defect in development, such fibrous support is wanting. In a case published in the *Anatomical Journal* for April 1923, I have shown to how great an extent the dextral cavities may become dilated under these circumstances, and alone account for the death of the subject. Efficient valvular action is not the negligible factor which it was at one time supposed to be. This is an important fact for, as is well known, some incompleteness at times of auriculo-ventricular closure in this situation has been maintained by some to be physiological, and was, I believe, first suggested by John Hunter. Kurschner (*Wagner's wörterbuch d. Physiol.*) commenting on the musculature of the valves, points to the peculiarity of the mechanism of right auriculo-ventricular closure in the bird in support of this contention.

A definite local nervous control in the heart does not, as we know, at present find much favour with the physiologist, as I have already stated, and this is one of those points on which the quality and character of specialised structural mechanism, from an anatomical point of view, must be advanced as awaiting recognition by him, before he can accept the neural relations indicated.

Auriculo-ventricular sphincteric action is the final phase of auricular systole and must, from anatomical conditions demonstrable, be maintained during ventricular systole, *i.e.*, when general auricular systole has given place to diastole. What, then, becomes of the "all or none" hypothesis of cardiac muscular contraction?

The final sphincteric phase of auricular systole has, manifestly, as its object, not only the prevention of reflux from the systolic ventricle, but the maintenance of lower auricular closure while this chamber is filling. The complete circular lower auricular muscle of the fish, which I have already mentioned, indicates this very clearly, and sections of the mammalian heart (mouse) prove the same fact.

It is clear that the lower auricular sphincter cannot act during the main systole of the auricle, as the effect would be to obstruct the flow of blood from auricle to ventricle. It must therefore act when the chamber has been emptied, that is, after auricular systole, certainly during the short pause, and the anatomical conditions indicate also during ventricular systole. Its motor innervation is probably sympathetic.

The local nervous cardiac control suggested may be regarded

as a modification of vaso-motor action, just as the striped muscle of the heart is a transitional condition between the usual unstriped visceral muscle fibre and voluntary muscle. However heretical the suggestion of such local nervous control may be, it is merely a reversion to the view once generally held of a certain visceral ganglionic or centro-peripheral autonomic control. If physiological observation and interpretation reject such a view, I would with all deference maintain, that in the muscular mechanism, anatomical facts appear to support it. This conclusion calls in question views at present generally accepted of the myogenic nature of many cardiac irregularities of action.

The neural relations of the cardiac muscle is too large a subject to be treated incidentally in this paper, but we now know every element in the latter, originative and executive, to be fully innervated, a fact once denied, and the central relations of the peripheral visceral system are beyond question. I am quite aware, however, that in my present contention I may find little support at this time.

From the clinician's point of view, this lower auricular action is important. It is more difficult for the auriculo-ventricular sphincter to act perfectly when the valve is stenosed than when it is merely incompetent. The force of reflux in the latter case is dependent upon the degree of incompetency and the strength of ventricular systole. This is true likewise of stenotic lesions as regards the degree of narrowing; but impeded exit of blood from the auricle interferes with the perfect systole of that chamber to a greater extent than does the intermittent systolic pressure of ventricular blood upon the largely closed auricle in ventriculo-auricular regurgitation, and mitral stenosis is, *par excellence*, the lesion most frequently associated with auricular fibrillation.

The transmission of reflux vibrations into the auricle, and their audibility in the back, are a measure of the degree of mitral incompetency. For, even loud presystolic bruits, with vibrations passing towards the ventricle, are inaudible posteriorly. When, moreover, in the paretic auricle in a state of what we have come to term fibrillation this auricular sphincteric action is in abeyance, reflux from the ventricle is favoured, even when there is no structural disease of the auriculo-ventricular valves. This may be observed, for example, in the later stages of Graves' disease when the auricle is fibrillating and the mitral valve becomes incompetent.

II.—The Auriculo-Ventricular Orifice.

As Noël Paton has shown (*Trans. Roy. Soc. Edin.*, 1892; *Rep. Roy. Coll. of Phys., Edin.*, vol. iv. p. 36), the approximation and tightening of the auriculo-ventricular segments in ventricular systole completes the occlusion of the orifices in question, and helps to guard against reflux under normal conditions. This tightening as well as approximation of the valve segments has been referred to before, but the medium of tightening has been ascribed chiefly to the papillary muscles in systole, and that they are agents in this action is probable. But there appears also to be a specialisation of ventricular muscle at the base of the segments, certainly of the mitral segments, which pulls in systole in a direction opposite to papillary action. I show this mechanism in my sections (Fig. 3), and do not know of attention to this point having previously been drawn. Such approximation is also brought about by the sphincteric action of the lower auricular segment already referred to. At the right auriculo-ventricular orifice this special mechanism is not so evident, and the difference in intra-ventricular pressure between the right and left chambers of the heart, together with the relations of the former to the pulmonic circulation, probably account for the distinction.

III.—The Ventriculo-Arterial Outlets.

I come now to the consideration of the anatomy of the ventriculo-arterial mechanism. The physical conditions and action of the conus ventriculi dextri and the musculature of the valves of the pulmonary artery differ from those obtaining in the left ventricle at the aortic orifice.

The simultaneity of right and left ventricular action is generally maintained by physiologists, but the clinician is familiar with a reduplication of the first sound of the heart on auscultation, while a reduplication of the second sound, in retarded states of the pulmonic circulation, as in mitral stenosis, is a very common phenomenon. It may also be seen in that interesting photographic process of so-called "retarded cinematography," that the contraction of the right ventricle and conus arteriosus precedes that of the left ventricle. This is not a matter of opinion. It is an observable fact.

Unlike the aortic valves, the valves of the pulmonary artery

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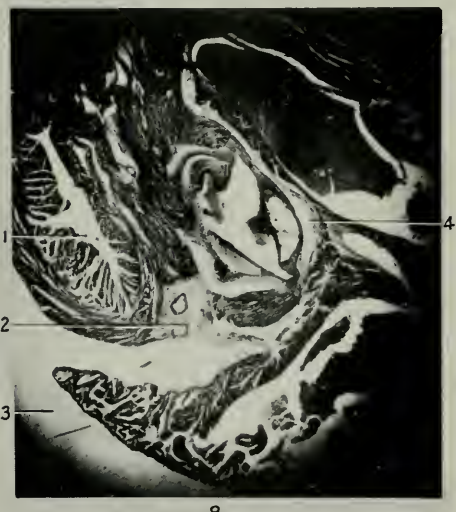

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FIG. 5.—1. Left anterior aortic cusp. 2. Rotator tendon beginning to be clothed with muscle. 3. Posterior aortic cusp. 4. Left auricle. 5. Right auricle.

FIG. 6.—Mouse. 1. Left anterior aortic cusp. 2. Left coronary artery. 3. Rotator tendon more clothed. 4. Left auricular appendix. 5. Posterior aortic cusp.

FIG. 7.—Mouse. 1. Right anterior aortic cusp. 2. Left anterior aortic cusp. 3. Left coronary artery. 4. Posterior aortic cusp. 5. Rotator still more clothed.

FIG. 8.—Mouse. 1. Conus arteriosus. 2. Rotator aortae. 3. Left auricular appendix. 4. Posterior aortic cusp.

have no connection with auricular musculature, but, as in the bulbus arteriosus of selachian fishes, the cardiac musculature reaches to just beyond the level of the pairs of valves. The mammalian conus thus has a detrusive action on this orifice in systole, and spreads and supports the anteriorly placed segments in diastole. This detrusive and supporting action of the conus elucidates some physical phenomena in clinical medicine, such as the systolic pulmonary arterial bruits commonly met with in chlorotic patients, the accentuation of the pulmonary arterial second sound in impeded states of the pulmonic circuit, already referred to, and, though more rarely, even a diastolic functional bruit when these pulmonary valve supports have yielded. The support of the deep or posterior cusp by the inter-ventricular septem renders it a fixed point, and any dilatation of the orifice must therefore occur anteriorly, where the valves are supported by the more yielding musculature of the upper and anterior wall of the conus. The superficial position of the pulmonary arterial cusps, apart from their situation behind the third left costo-sternal junction, or the adjoining third inter-costal space when distended and displaced, causes physical signs arising from them to be more easily heard by the ear and felt by the hand, than those due to conditions in the deeper lying aortic valve. In the case of the latter vessel, the second sound of the heart is often best heard above the clavicle or in the supra-sternal fossa, that is, by way of the larger arterial trunks leaving the aortic arch. As a clinical fact in the case of stout patients, or in those with emphysema of the lungs, this is important.

Morphologically, the conditions at the origin of the pulmonary artery resemble more closely the arterial mechanism of the selachian than the teleostean fish, the dog-fish rather than the trout, the mechanism in the latter being a closer approach to that found at the mammalian aortic orifice. There is but one series of aortic valves in the latter, and it is not embraced by cardiac muscle.

In all that has been stated so far, with the exception of the mitral valve-tightening mechanism at the auriculo-ventricular orifice, by fibres attached to the base of the segments, and imbedded in the ventricle, and the emphasis laid upon the power and duration of the final sphincteric phase of auricular systole, as having for its object both the filling of that chamber and prevention of regurgitation from the ventricle, nothing has

been said which can be regarded as novel. But a muscular mechanism, active at the base of the aorta, to which I shall now call attention, has not, so far as I know, been previously described.

Everything bearing upon the structure and mechanism of the great systemic arterial outlet is important. This orifice is, so to speak, the muzzle of the arterial gun, and former writers (Pettigrew, Quain, etc.) have drawn attention to a so-called rifle or rotational action of the left ventricle, as it discharges its contents through the aortic muzzle. Foster writes: "As the systole progresses, the aorta and pulmonary arteries expand and elongate, the apex is tilted slightly upwards, the heart twists somewhat on its long axis, moving from the left and behind towards the front and right, so that more of the left ventricle becomes displayed. As the systole gives way to the succeeding diastole, the ventricles resume their previous form and position, the aorta and pulmonary artery shrink and shorten, the heart turns back towards the left, and so the cycle is completed" (*Physiology*, 6th ed., p. 232). This depressive and rotational movement of the heart in systole is generally admitted. Were the base of the aorta in such movement fixed, while the ventricular mass rotated as described, or the whole force of ventricular systole were spent upon it, one can easily imagine an undue strain being placed upon the base of the vessel which, as we know, suddenly thins in texture about the level of the coronary arteries, and all ventricular musculature of the aorta is below the level of those vessels.

Serial sections, however, show the existence of a set of fibres belonging to the left ventricular musculature and also to the lower segment of the auricle, the effect of the contraction of which is to rotate the base of the aorta in the direction of the general ventricular twist in systole. Were this movement of the delicate aortic base brought about by the full force of general ventricular systole, it is quite conceivable that injury might be sustained by the structure in question. It is therefore not surprising to find a special provision for securing the harmonious twist of the aortic base, in consonance with the larger rotation of the heart. The interesting group of small ventricular muscles effecting this purpose might, indeed, be designated by a double diminutive, the muscululi rotatores basis aortae (for musculus itself is a diminutive).

Such limitation, specialisation, or control in action of portions

of a general muscle mass, if unrecognised by the physiologist at present, belongs to the category to which I have already ventured to refer, and the muscululi in question, if existent in anatomical fact, as they are, and from their structure and attachment indicating their function, must be left for future physiological recognition.

It is not suggested that these muscululi act independently of the ventricular mass in systole, but that their anatomical origins and attachments enable them to serve the purpose of moderators to the force and general effect of the larger ventricular action, and they are, like every fibre of the heart, completely innervated. They are a form of moderator bands, but so specialised as to suggest a special nerve control. I venture to submit this heresy of the moment, and leave it to be incorporated in the orthodoxy of the future. I show sections in support of my statements (Figs. 4 to 9).

Numbered from left to right, the first may be seen to arise from fibrous texture in the neighbourhood of the left coronary artery, and to be inserted by a beautifully shaped tendon into the base of the aorta at the left end of the posterior cusp, near its junction with the left anterior cusp. Serial sections made towards the ventricular cavity show a peculiar arrangement of the muscle fibres of the group. These do not pass into the general ventricular musculature, but rather acutely curve towards the left and anteriorly, and are inserted into the circumference of the aorta itself. This curving gives the impression of a digastric muscle, but without the intervening tendon, although there are strata of fibres which terminate in fibrous texture which appears to play the part of such an inter-tendon. As an anatomical entity or organ, the group appears to be as distinct as the stapedius muscle. The second group appears to be inserted at the junction of the right anterior with the left anterior cusp, and to arise near the edge of the ventricular cavity. The third is inserted near the same part of the aortic circumference as the second muscle bundle, and arises in fibrous structures near the right end of the posterior cusp. The posterior cusp itself is without nearer connection with these left ventricular grips in rotatory mechanism (if such it be), than the insertion of the muscle group most to the left, which was first described.

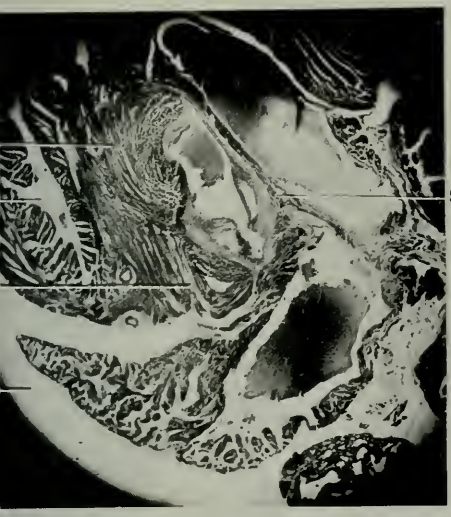
The posterior cusp is, however, not beyond the influence of special muscular action, but that influence is auricular, not

ventricular. Longitudinal or rather oblique sections show that the right end of the posterior cusp as it joins the aorta, and that vessel itself to the right of and below the cusp, are powerfully attached to the inter-auricular septem in such a manner that when it contracts in auricular systole, it must not only support the cusp and aorta during ventricular diastole by some of its fibres, when the blood weight is upon the aortic valves, but must also rotate the vessel somewhat in the same direction as the muscululi already described (Mouse, Fig. 10).

The examination after death of cases of longstanding auricular fibrillation commonly shows that when the aortic valves are themselves free from disease (as they usually are in such cases) the cusps are loose and baggy. This stretched and baggy condition of these cusps appears to be due to the same paresis of the lower auricular segment which, in the later stages of Graves' disease associated with fibrillation, permits of mitral reflux and, together with the general lack of co-ordinate contractile power on the part of that chamber, accounts for the diminished or lost audibility of the presystolic murmur of mitral stenosis.

The septal wall of the aorta is the line on which the heart moves and twists in systole from left to right, and an examination of its attachment to the inter-ventricular septem shows it to be stronger than the opposite segment of its lumen, resting on ventricular muscle, which is more mobile. It is the line not only of rotation but also of depression in ventricular systole, and of elevation or shortening in ventricular diastole.

Sections in the human subject through the posterior valve, made in such a manner as to include a portion of the supra-valvular aorta, the pars membranacea septi, the auriculo-ventricular bundle, and a part of the septum ventriculorum, show the insertion behind the aortic valve of longitudinal fibres of the auricle, which in auricular systole must elevate and support the base of the aorta and the aortic valves during ventricular diastole. Savory's description also shows this, and he was the first to study the subject by longitudinal section (Figs. 11 and 12). More anteriorly and to the right there is also powerful muscular attachment by ventricular fibres to the aorta in the line of the septum, which must during their systole help to depress the vessel as it is lowered and rotates, as already described during ventricular contraction; but the



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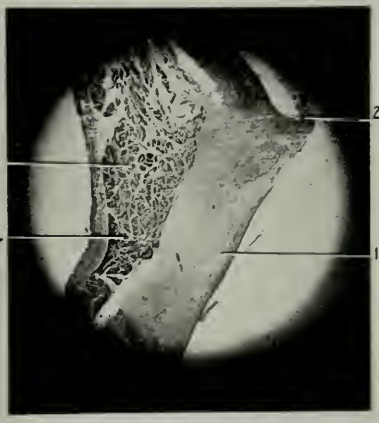

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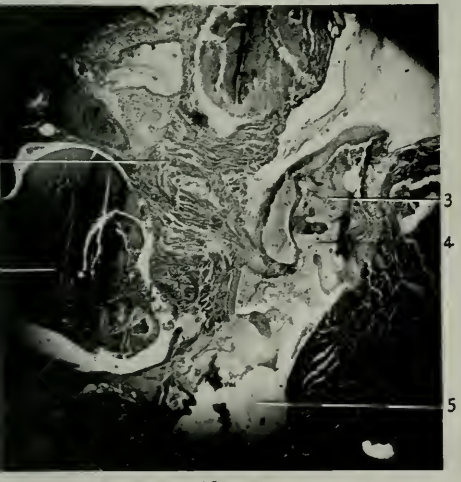

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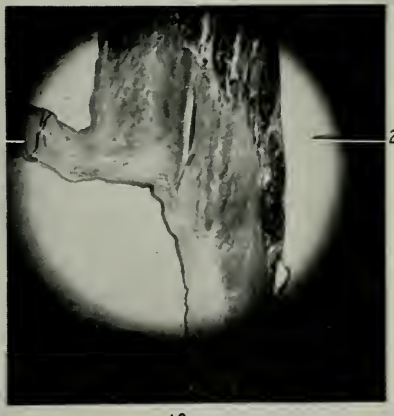

12

FIG. 9.—Mouse. 1. Anterior rotator 2. Conus arteriosus. 3. Posterior rotator showing opening into left ventricle. 4. Left auricular appendix. 5. Posterior aortic cusp.

FIG. 10.—Mouse. 1. Septum auricularum. 2. Right auricle. 3. Aortic cavity. 4. Posterior aortic valve cusp with auricular muscle entering it. 5. Left ventricular cavity.

FIG. 11.—Man. 1. Cusp of mitral valve. 2. Aortic cusp. 3. Auricular musculature. 4. Auricular muscle of coarse type in lowest segment.

FIG. 12.—Man. 1. Posterior aortic cusp. 2. Auricular musculature of aorta.

chief pull upon the aorta in this lowering and lengthening of the great arterial trunks during systole is, without doubt, the contraction of the ventricles and their septum themselves, just as the chief agent in the shortening of those channels is the release of the same structures in ventricular diastole. The support, during auricular systole, of the posterior aortic valve, and the related segment of the vessel in the period of ventricular diastole, remains therefore a function of some of the fibres of the auricular attachments to the aorta.

There has been some controversy as to whether the cardiac second sound is wholly explicable by the sudden opening of the cusps, to receive the blood weight during diastole. If Rosenbach be correct in supposing that they unfold gradually, as the aorta fills with blood during systole, he maintains that there is too little rebound possible to account for the production of the phenomenon in question by this mechanism, and that other explanation is required.

When, however, we bear in mind the movements of depression and release mentioned, and the support of the posterior segments of the vessel by auricular systole, the additional factors necessary to produce the vibration causing the second sound appear to be provided.

The conditions at the pulmonary arterial orifice, as already stated, are not quite the same as in the case of the aorta. Here, the posterior cusp is that most solidly based upon the ventricular septum, and there is a greater muscular control both in folding and unfolding the valves in systole and diastole respectively. The notable accentuation, moreover, both in aortic rigidity and in impeded pulmonary circulation, declare the accepted view of the production of the second sound to be essentially correct.

Summary.—What has been said may be summarised as follows :—

1. The occlusion during upper auricular systole, of the superior vena cava, is by a sphincteric action of the lower end of that powerfully muscular vessel, which is influenced by the innervated sino-auricular node.

2. The coronary sinus is also a para-auricular body, guarded from reflux into it from the auricle by its proper valve (the Thebesian), and by contraction of the auricular fibres at its orifice. It is the venous heart of the coronary system.

3. The inferior vena cava is closed by the systolic auricle rendering the Eustachian valve efficient.

4. Auricular closure is also the mechanism of occlusion of the pulmonary veins.

5. The final phase of auricular systole is the chief muscular mechanism for closure of the auriculo-ventricular valves, and its special object is not only the prevention of regurgitation from the ventricle but the filling of the auricle.

6. The tightening of the segments of the approximated auriculo-ventricular segments during ventricular systole, as is best seen in the left heart, is not only ventricular papillary but also basic, by a specialisation of ventricular muscle.

7. The pulmonary arterial orifice has a mechanism more analogous to that of selachian than teleostean fishes, the latter having a closer analogy with the conditions obtaining at the aortic orifice.

8. There is a group of small muscles, the musculi or muscululi rotatores basis aortae, the function of which is, in agreement with general ventricular systole, to rotate the base of the aorta from left to right.

9. The posterior aortic wall is musculated by the septum auriculorum, the effect of the auricular systolic contraction of these fibres being to support the aortic cusps during ventricular diastole.

10. Auricular musculature of the posterior aortic valve by the lower auricle also appears to act in unison with the ventricular aortic rotators described, during ventricular systole.

11. The chief agents in the lengthening and shortening of the great basic arterial trunks during the cardiac cycle, are the contraction and release of the ventricles and their septum, during ventricular systole and diastole respectively.

12. The centro-peripheral innervation of the heart is, in its nature, transitional between visceral vaso-motor and somatic innervation, and the evidence for this is, specialisations in the cardiac musculature, the functions of which are anatomically indicated.

13. Cardiac acceleration, augmented action, some forms of cardiac retardation, auricular fibrillation, and extra-systoles both rhythmical and arhythmical, are quite as validly explicable on a neural as on a muscular hypothesis, both the inhibition and motor innervation of the heart being highly developed.

Note.—I am indebted to my House Physician, Dr Reena Maclennan, for the micro-photographs and lantern slides

illustrating this paper, and to Mr George French, Assistant in the Pathological Department of the Royal Northern Hospital, for the microscopic sections which he prepared under my supervision.

Discussion.

Professor Russell said he was sure the Society must be gratified that Dr Blackhall-Morison had considered it a duty and a privilege to submit to them the interesting and important piece of original investigation which he had expounded to them. He would not attempt to criticise the anatomical side of the work: he had to leave that to those who were more competent. The work appealed to him very strongly and had the effect of filling in detail of great value and interest to the mental picture he had formed of the living mechanism of the circulation.

Dr W. T. Ritchie considered that the musculature at the lower end of the superior vena cava must play an active part in the closure of that vein during auricular systole. Defective tone of the portion of auricular musculature extending into the mitral valve, and of the mitral sphincter, could cause functional mitral murmurs. Gibson's researches on the difference between the pulmonary and aortic sphincters explained why functional incompetence was frequent at the former, but rare at the latter orifice.

A CASE OF EXTENSIVE RESECTION OF SMALL INTESTINE, WITH A CLINICAL STUDY OF RECORDED CASES.*

By PIRIE WATSON.

THE case now recorded—fully three years after resection of 228·5 cm. (7½ ft.) of small intestine (ileum), is of interest as a recovery from a dangerous pathological lesion as well as from a severe abdominal operation; is of interest also because the patient early regained her former good health and strength, and up to the present has suffered from no nutritional disturbances.

CASE—*Clinical Record.*—Mrs S., age 63, a patient of Dr W. Stewart of Leith, was admitted to Leith Hospital on the forenoon of the 13th April 1920, as an "acute abdomen." At 10 P.M., on the previous night she had been seized suddenly with acute pain in the region of the umbilicus accompanied by continuous vomiting. The last evacuation of the bowels occurred on the 11th, and for two days neither fæces nor flatus had been passed. There was no history of previous ill-health or constipation or of heart or lung trouble; she had always been a healthy woman. On admission she looked pale and ill, with a drawn, anxious expression, and complained greatly of abdominal pain. She was thin and frail-looking for her age. The vomiting was fairly frequent, and the brownish fluid vomited had a slight fæcal odour. Her temperature was subnormal—97° F.; pulse 76; respirations 20. The abdomen was only moderately distended, and several coils of intestine were prominent through the thin abdominal wall, but there was no visible peristalsis. The hernial openings were examined, but no sign of hernia discovered. A rectal examination revealed a fullness in the pouch of Douglas. The heart and lungs were apparently healthy. An enema was given and returned unchanged, and no flatus was passed. The diagnosis of acute intestinal obstruction was easily made, but the cause was not so apparent. Volvulus was suspected. Operation was immediately performed under ether anæsthesia. An incision was made below the umbilicus and to the left of the mid line, the left rectus was retracted laterally and the abdominal cavity entered. Blood-stained fluid was present in quantity and several coils of small intestine were found deeply congested, dark red with black patches and obviously becoming gangrenous. There was no volvulus, no internal hernia, no strangulating band. The mesenteric blood-vessels were thrombosed to the extent of fully 2 in.

* Read 6th June 1923.

from the attachment of the mesentery to the affected bowel. The gangrenous small intestine was found to be ileum, to be almost sharply defined proximally, but gradually to merge into healthy bowel at its distal end about 18 in. above the ileo-cæcal junction. The line of demarcation above was somewhat narrowed, but no constricting band was found and no evidence of old adhesions. Embolism or thrombosis of branches of the superior mesenteric vessels was considered the probable cause, although there was no obvious cardiac lesion and no cirrhosis of the liver so usual in such cases.

At this stage of the operation the patient's general condition gave much anxiety, but was distinctly improved on the administration of saline subcutaneously by Dr W. Stewart of Leith who was present at the operation. Meanwhile, the gangrenous bowel was resected well beyond the apparent limits of the affected area, the ends closed and invaginated, a lateral entero-anastamosis made and the V-gap in the mesentery closed. The peritoneal cavity was filled with saline and the abdomen closed by layers with a drain at the lower end of the incision down to the pouch of Douglas. Rectal salines were given four hourly during the first twenty-four hours, along with 1 c.c. pituitrin hypodermically, and her general condition rapidly improved. A flatus enema on the evening of the third day gave great relief, and 5 grains of calomel were given followed by a seidlitz. On the fourth day she had several attacks of severe vomiting, which ceased after the bowels had been well opened by an enema. On the fifth day calomel was again administered and one motion resulted. During the next fourteen days the bowels opened two, three, or four times a day, with occasionally a day when one or no motion was recorded. Thereafter the motions numbered usually one and occasionally two or three each day. There was therefore no excessive frequency. In character the motions were soft in consistence and partly fluid, of good colour, and rather offensive in odour. Her general condition rapidly improved, her convalescence was uneventful, and the abdominal wound healed rapidly. She was allowed up on the twenty-first day, and discharged from hospital on the twenty-eighth day. Her appetite was good, but not increased. In hospital she had been latterly on light convalescent diet, but she remembers that her first meal on her return home consisted of ham and eggs which produced no ill effects. She soon regained her former weight and strength, and at an early date resumed her household duties, which are performed without assistance and include a heavy weekly washing of clothes—a sufficient test of the completeness of her recovery. On several occasions I have visited her and found her in good health and busy at work. In answer to my questions on a recent visit she states that she never enjoyed better health than at present; her appetite is good but has never been excessive, not even during the months

immediately following her operation. Her weight has remained steady. She has never suffered from diarrhœa, and is never constipated. Her bowels open once every morning, and only very occasionally does she take a mild aperient pill. Since her return home from hospital she has eaten the ordinary food taken by the rest of the family, and she knows of no food that in her case causes looseness of the bowels. She takes soup or broth nearly every day, and does not avoid fatty foods any more than she did before the operation. There have been and are now no symptoms of nutritional disturbance. Her fæces are soft, but formed with only a few oily globules throughout, well coloured, but not more offensive in odour than normal. A specimen of the fæces after her ordinary diet was examined by Professor Meakins and his staff at the Bio-Chemical Laboratory in the Royal Infirmary of Edinburgh, and the report is as follows:—"Total fat is rather low 18 per cent. (normal 25 per cent.), ratio of free fatty acids and soaps to neutral fats is normal. The nitrogen excretion is about normal for mixed diet."

For further investigation into the nitrogen excretion the intake would require to be known. I have endeavoured to persuade the patient to enter hospital so that she could be given a known diet and the nitrogen waste examined. This she has not consented to do, but the above result is practically normal, and as she has no metabolic disturbances further investigation would not likely produce any different result.

Her urine shows a very slight excess of indican, but no increase in ethereal sulphates. There is therefore no indication of increased putrefaction in the intestinal contents.

Definition of Term "Extensive."—By growing consent the term "extensive" (or long) is applied to resections of small intestine measuring from 200 cm. (6 ft. 7 in.) and upwards. This measurement is arbitrary and artificial, but the study of clinical records shows 200 cm. to be the limit in resection beyond which serious metabolic disturbances may result. The normal small intestine varies much in length—from 15 ft. 6 in. to 31 ft. 10 in.—according to Treves, who stated 22 ft. 6 in. as the average length in the adult male and 23 ft. 4 in. the average length in the adult female. Treves obtained this average from measurements of 100 cases. He believed that age, height and weight do not influence the length of the small intestine. Beneke, on the other hand, states that for every 100 cm. (3 ft. 3½ in.) of body length there is 387·5 cm. (12 ft. 9 in.) of small intestine, and Flint supports the view that there is a definite ratio between the size of the organism

and the epithelial surface of the intestine. There seems evidence to show that diet may influence the length of the small intestine. Russians and Italians who live on a bulky vegetable diet seem to have a longer intestine. Babák, experimenting on frog larvæ, found that those fed on a vegetable diet had larger intestines than those fed on a meat diet.

In Gray's *Anatomy* the average length is given as 6 metres (19 ft. 19 in.). Jonnesco gives $7\frac{1}{2}$ metres (24 ft. 7 in.) as the average, and Keith, in the *British Medical Journal* of 1st April 1922, stated $22\frac{1}{2}$ ft. as the average of the small intestine.

Thus the resection of 200 cm. (6 ft. 7 in.) may equal almost half the length of the small bowel or only about one-fifth, but on the average almost equals one-third. The term "extensive" therefore is applied to resections of one-third or more of small intestine.

Recorded Cases—73.—Cases of extensive resection of small intestine with recovery have been recorded from time to time, but the total number—73—(including my own case now recorded) is still comparatively small.

Dreesman, in 1899, collected 26 cases, but in only 7 of these did the resection exceed 200 cm. Blayney, in 1901, added 7 more cases to Dreesman's table, but only 1 of these 7 (Hayes' case, which he records) exceeded 200 cm. Schlatter, in 1906, collected records of 20 cases, and Storp, in 1907, 22 cases, and these tables are almost identical.

Flint, in 1912, collected 59 cases, with 48 recoveries. Moynihan, in 1918, collected 54 cases, with 53 recoveries. Cannaday, in 1919, tabulates 69 cases (including 1 of his own), with 60 recoveries. Cannaday's collection includes all Moynihan's and all Flint's except 2 (1 a resection of 100 cm. and the other a short circuit without resection). In 1919, Littlefield recorded a case of resection of ileum, measuring 13 ft. ($396\frac{1}{2}$ cm.), with recovery. In 1920, Quarry Wood published his case of resection of ileum, measuring 7 ft. 2 in. (218 cm.), with recovery. Including my own case here recorded the total number of cases published where the resection of small intestine exceeds 200 cm. is 73, with 64 operative recoveries.

The natural tendency is to record only successful cases in which there is a recovery lasting over several months or years. This accounts for the astonishingly low death rate in the published cases—12·3 per cent. The percentage of

recoveries from the operation equals 87·6, and the percentage of good functional recoveries is 64 per cent. There must, of course, be a large number of cases of extensive resection not recorded because of an immediate or rapidly fatal ending. The surprise is that so many cases with recovery have been recorded following an operation which would be severe in the perfectly healthy, and which is so much more severe in the presence of the extensive pathological conditions which necessitate such free removal of bowel.

A survey of these recorded cases reveals many points of interest. The earliest case, as regards date, is Kœberlé's recorded in 1881, where 205 cm. (6 ft. 9 in.) of small intestine were removed from a woman, aged 22, for multiple strictures. Recovery was followed by no digestive disturbances. The longest resection is Brenner's case, reported by Denk in 1910, where 540 cm. (17 ft. 9 in.) of gangrenous bowel were removed from a strangulated femoral hernia. The patient, a woman aged 61, made an excellent recovery for a time, but eventually died of marasmus two and a half years later.

Age.—The ages in these tabulated cases vary widely. Flint, in 1910, resected 100 cm. of ileum from a male infant, aged 11 months, for intussusception with gangrene. Flint includes this case in his series because the small intestine in infants of this age is only 9 ft. long, and therefore the resection of 100 cm. (3 ft. 3½ in.) is equivalent to the arbitrary limit of 200 cm. (6 ft. 7 in.) taken in adults. In spite of the severity of the operation the infant made a splendid recovery, although for the first fourteen days there was marked diarrhœa showing severe metabolic disturbances.

Ruggi recorded, in 1896, the resection of 330 cm. (10 ft. 10 in.) of ileum from a boy, aged 8, who made a good recovery Hayes, in 1900, resected 255 cm. (8 ft. 5 in.) of ileum from a boy, aged 10, who recovered, but suffered from occasional diarrhœa and vomiting and developed chorea. At the other extreme, as regards age is Lauwer's case, recorded in 1901, in which 265 cm. (8 ft. 9 in.) of small intestine were resected, from a woman, aged 65, for ventral hernia with intestinal obstruction from adhesions. She recovered. Fantino recorded, in 1896, the resection of 310 cm. (10 ft. 2 in.) of ileum from a man, aged 60, who had a large inguinal hernia with volvulus of intestine and gangrene. He recovered, and was in good

general condition one year later. Quarry Wood, in 1915, resected 7 ft. 2 in. (218 cm.) of gangrenous ileum from a woman, aged 62, with a strangulated umbilical hernia. She survived two years, ultimately dying of bronchitis. My own case of extensive resection occurred in a woman, aged 63, from whom 228·5 cm. (7 ft. 6 in.) of ileum were removed for gangrene following mesenteric thrombosis. She is still alive and well, three years after, and suffers from no metabolic disturbances.

Brenner's case, the *longest* resection as yet recorded, 540 cm. (17 ft. 9 in.) was a woman, aged 61, with a strangulated femoral hernia with gangrene. She recovered, maintained her weight, was able to do her housework without fatigue, and lived for two and a half years, eventually dying of marasmus.

Flint found that young, growing animals do not stand the operation so well as older dogs, but from a consideration of the ages in this series it follows that recoveries from extensive intestinal resection have resulted in patients of all ages, from 11 months up to 65 years of age. In this series of 73 cases the ages are recorded in 36, and most of the cases occurred between the ages of 20 and 40.

Sex.—As might be expected, a study of sex, where stated in the recorded cases, reveals nothing of importance. In this series of 73, 24 cases are known to have been males, with 23 recoveries, and 15 are known to have been females, all of whom recovered.

Morbid Conditions.—The necessity for extensive resection of small intestine arises almost without exception in the course of an emergency operation in which the choice lies between closing the abdomen with the inevitable death of the patient, or resecting the diseased or injured bowel as the only chance of preserving life. In 54 out of this series of 73 the morbid conditions found at operation are stated, and include a wide variety of abdominal lesions.

19 cases were strangulated herniæ :—7, variety not stated ; 7, inguinal ; 2, femoral ; 2, umbilical ; 1, ventral.

8 cases were for strangulation from omental and other bands and adhesions.

8 cases were for trauma :— 3, rupture of mesentery and intestine ; 3, rupture of uterus, with protrusion of intestine ; 2, gangrene after intestinal prolapse through a punctured wound.

7 cases were for abdominal tumours:—5 of the mesentery, fibroma, myxo-fibroma, myxo-sarcoma, sarcoma; 1, ovarian; 1 carcinoma of cæcum, with metastases in mesocolon and mesentery.
4 cases were for multiple strictures (tuberculous).
3 cases for mesenteric thrombosis.
3 cases for volvulus.
1 case for intussusception.
1 case for gangrene of the bowel following appendicitis.

These cases cover a wide range of abdominal catastrophes.

The chance of recovery may be small, but the fact that 64 recovered out of 73 recorded cases (operative recoveries = 87·6 per cent., good functional recoveries = 64 per cent.), proves that the chance does exist and should be given. The recovery must be often a matter of surprise to the surgeon (as it was in my own case) and as it was to me, in reading the reports of the other cases.

Methods of Operating.—The method of restoring the continuity of the bowel is recorded in 35 of the 73 cases:—

(1) End to end anastomosis:—19 cases (13 by suture; 6 by Murphy button).

All these cases occurred between 1894 and 1909. There was one death within twenty-eight hours from collapse (Obalinski's case, 1894).

(2) Lateral anastomosis after both ends had been closed:—11 cases (9 by suture; 2 by Murphy button). The 9 suture cases occurred between 1896 and 1920. The 2 by Murphy button occurred between 1905 and 1906. There were no deaths in this group.

(3) End to side anastomosis:—2 cases (Brenner, 540 cm., in 1910, and Littlefield, 396 cm., in 1919). There were no deaths.

(4) Anus præternaturalis occurred in 3 cases:—

(*a*) Kœberlé's case, in 1881, spontaneous healing occurred.

(*b*) Maydl's case, in 1900. This patient died in three weeks, and the autopsy showed advanced tuberculosis of lungs, and abscesses were found in the pelvis.

(*c*) Quarry Wood's case, in 1915, where the fæcal fistula closed early after lateral anastomosis had been made.

From this survey it will be noted that end to end anastomosis was done in more than 50 per cent. of the 35 cases, but that lateral anastomosis by suture is favoured by more recent operators.

It is interesting to note that the 8 cases in which Murphy's button was used occurred between 1901 and 1909, and that there were no deaths in this group.

Parts resected.—In experiments on animals Trzebicki in 1894, stated that resection of the jejunum caused more profound loss in weight than resection of the ileum.

On the other hand, Diliberti-Herbin, in 1903, found no difference in results from resecting the upper half of the small intestine in one dog and the lower half in another. Both dogs at first showed lack of assimilation of nitrogenous foods and fats but gradually improved, gained weight, and recovered perfectly.

The evidence, therefore, from experiments on animals is contradictory. From the physiological point of view resection of the jejunum might be expected to cause more serious digestive disturbances than resection of the ileum.

The part of the small intestine resected is definitely stated to have been ileum in 25 of the 73 cases under review, and in only two of these 25 was jejunum included.

These two cases are extremely interesting:—

(1) Storp's case, in 1907—a male, aged 21, with sarcoma of the mesentery—510 cm. (16 ft. 9 in.) were resected, the entire ileum and part of the jejunum—continuity restored by primary circular suture. At first, slight diarrhœa, two to three soft stools daily. Three months later general condition good; 5 kilos increase in weight—normal defecation. Microscopic examination of stools showed more fat and fatty acid crystals than normal. Unfortunately, extensive recurrence of sarcoma with multiple metastases occurred five months after operation.

(2) Littlefield's case appears even more remarkable, for he states that the amount of bowel left was 6 in. of jejunum and 4 ft. of the ileum after resection of 13 ft. (396.5 cm.) of small intestine for gangrene from adhesions following an operation on pus tubes. This woman was aged 22, and her weight before operation was 110 lb. and three months after operation 109 lb., *i.e.*, one pound of loss—which is negligible.

She resumed her housework and ate well, but was apt to suffer from abdominal pains after coarse foods and pastries. Such pains have been felt by normal people after eating pastries, so that the disturbance appears astonishingly slight.

The clinical records therefore appear to support Diliberti-Herbin's statement that resection of the jejunum is no more serious than resection of the ileum.

Lengths resected.—The amount of intestine requiring resection in desperate cases is determined by the extent of the disease or injury, and as Kocher says: "It is important to know that such very extensive resections can be performed without harm and with uninterrupted recovery, because the first rule in intestinal, as in stomach, resections is this—only to suture together wound edges which are thoroughly well nourished." In this series of 73, there were 64 operative recoveries and 9 deaths.

In 41 cases the length resected was between 200 and 300 cm. (*i.e.*, 6 ft. 7 in. to 9 ft. 10 in.). Eight are definitely stated to have had no digestive disturbances, and 5 are definitely stated to have been in good general condition. There were 4 deaths, and one died of marasmus seven and a half months later.

In 26 cases the length resected lay between 301 and 400 cm. (*i.e.* 9 ft. 10 in. to 13 ft. 2 in.) with 5 deaths, although 2 others died of marasmus within a year. Seven had no digestive disturbances, and 5 continued in good general condition.

In 6 cases the resection measured between 475 and 540 cm. (*i.e.*, 15 ft. 8 in. to 17 ft. 9 in.). All six recovered from the operation. Three continued in good general condition, and the fourth had only slight disturbances. The fifth died in six months from pulmonary tuberculosis, and the sixth (Brenner's case, 540 cm.), the longest resection ever recorded, made a good recovery for a time, but died from marasmus two and a half years later.

Total No.	Length Resected.	After Reports. No. of Cases.	No Nutritional Disturbances.	Good General Condition.	Good Functional Recoveries.
41	200 to 300 cm. 6′ 7″ to 9′ 10″	21	8	5	$\frac{13}{21}$ = 62 %
26	301 to 400 cm. 9′ 10″ to 13′ 2″	20	7	5	$\frac{12}{20}$ = 60 %
6	475 to 540 cm. 15′ 8″ to 17′ 9″	6	...	5	$\frac{5}{6}$ = 83·3 %
	Total . .	47	15	15	$\frac{30}{47}$ = 64 %

Date of Reports after Operation :

14 years	Zusch	General conditions good.	
7 „	Schlatter	„	„
6 „	Monprofit	„	„
5 „	Goebell	„	„ excellent.
3 „	Pirie Watson	„	„ „
2½ „	Kukula	„	„ good but recurrence of tumour.
2½ „	Brenner	„	„ „ but eventually died from marasmus.

The lengths resected therefore vary between 200 cm. and 540 cm. (*i.e.*, between 6 ft. 7 in. and 17 ft. 9 in.).

Taking the average length of the small intestine as 22½ ft., these resections vary from roughly 30 to 80 per cent. of the entire gut.

It is worthy of note that in the six longest resections there were no operative deaths, and only one death directly due to inanition following the loss of bowel, and that two and a half years after the operation. These results are astonishingly good.

Metabolic Disturbances.—Out of the 73 cases no metabolic disturbances occurred in 15 cases, and 15 others are reported as in good general condition. In 26 cases there is no report on the after-condition, so that the average of good functional recovery is 64 per cent. (*i.e.*, 30 out of 47).

Diarrhœa occurred in 13 cases, in 5 at first only, in 4 others after certain foods only; in one with some loss of weight, in another with gain in weight, and in two resulting in death from marasmus, seven and a half months and twelve months after the operation.

Diarrhœa is the commonest manifestation of disordered metabolism in these cases. It was also the commonest symptom in the dogs which had been subjected to extensive resections.

Offensive stools is specially mentioned in one case, but was commonly found in the animal experiments, and is due to the putrefaction of undigested food which has remained for a longer period in the large intestine under the altered circumstances. Soft and pulpy stools occurred in two cases, the one gained in weight and the other continued in good general condition. Increase of appetite is mentioned in two cases only, but in animal experiments a ravenous appetite is a prominent symptom.

Death from marasmus occurred in 6 cases :—

1.	350 cm.	25 days after operation.
2.	300 „	1 month „
3.	315 „	3½ months „
4.	289 „	7 „ „
5.	400 „	12 „ „
6.	540 „	2½ years „

Amount Resected.	No. of Cases.	Operative Recoveries.	Operative Deaths.	No Metabolic Disturbances.	In Good General Condition.	No After Report.	Diarrhœa.	Offensive Stools.	Increased Appetite.	Marasmus.	
192 to 250 cm. 6′ 4″ to 8′ 3″	26	24	2	6	5	13	4 (3 slight)	...	...	...	1 died from peritonitis. 1 died from violent metabolic disturbances.
251 to 300 cm. 8′ 3″ to 9′ 10″	15	13	2	2	...	7	2 (1 at first only, 1 afterwards marasmic)	1	1	2	1 died following operation. 2 died within 2 months from pulmonary tuberculosis. 2 died from inanition (1 in 1 month, 1 in 7 months).
301 to 350 cm. 9′ 10″ to 11′ 6″	17	15	2	4	5	4	3	...	...	2	1 died in 2 days. 1 died from inanition in 25 days. 1 died from inanition in 3½ months.
351 to 400 cm. 11′ 6″ to 13′ 2″	9	6	3	3	...	2	3	...	...	1	3 died following operation. 1 died from inanition within 1 year.
475 cm. 15′ 8″	2	2	...	...	1	...	...	...	...	...	1 died in 6 months from pulmonary tuberculosis, but maintained weight for 3 months.
510 to 540 cm. 16′ 6″ to 17′ 9″	4	4	...	(1 slight)	4	...	1 at first, later normal defecation	...	...	1	1 died 5 months later from recurrence of sarcoma. 1 died from marasmus 2½ years after operation.
Total . .	73	64	9	15	15	26	13	1	1	6	

Cases with special Metabolic Investigation.

No.	Operator.	Resection.	Time after Operation.	Nitrogen Residue.	Fat Residue.	Remarks.
1	Schlatter, 1899	192 cm.	5 weeks	Normal	Double average	7 years later condition good, with light work and careful diet. Tendency to diarrhœa after eating milk polenta and fruit.
2	Lexer, 1900	200 cm.	1½ years	Normal	Normal	2 years after operation. General condition good. No digestive disturbances.
3	Pirie Watson, 1920	228·5 cm.	3 years	Normal	Slightly below average	No digestive disturbances. Eats ordinary food. Fully able to work.
4	Fantino, 1896	310 cm.	18 days	Very great (23 %)	Very great (29 %)	Increased defecation, but no emaciation on account of increased nourishment. General condition good a year later.
5	Zeidler, 1906	318 cm.	2 months	Above normal	...	General condition good 2 months later, and reported to be quite well 1 year later.
6	Miyaki, 1912	328 cm.	2 months	Stated to be normal 29·8 %	Stated to be normal 31·7 %	At first three stools per day; 7 months later one or two formed stools. Had gained 9·5 kilos in weight.
7	Ruggi, 1896	330 cm.	1 year	Normal	Normal	General condition good 1 year later.
8	Axhausen, 1909	475 cm.	16 days	34·2 %	36·5 %	Maintained weight during 3 months. Death 6 months later from pulmonary tuberculosis.
9	Nigrisoli, 1902	520 cm.	From 22nd day for 23 days	At first great loss, rapidly became nearly normal.	At first great loss, rapidly became nearly normal.	5·1 kilos gain in weight during the 23 days. Continued in good condition. Defecation almost normal, though at first stools slimy and watery.

Special *investigations into nitrogen and fat residue* in the fæces are reported in 9 cases (p. 175).

The nitrogen residue was normal in 6, increased in 3, but became normal in one of the three later.

The fat residue was normal in 4, increased in 4, but in one became normal later.

When examination of the fæces was made a few weeks or months after operation, the loss of nitrogen and fat was in excess, but when examination was made a year or more after the operation, the loss of nitrogen and fat was normal in amount. This points to a compensatory process taking place, slowly but certainly, under favourable conditions, and is quite in accord with the findings from experiments on animals.

The metabolic disturbances are not uniformly in proportion to the amount of intestine resected. Severe digestive disturbances followed the resection of 192 cm. in Schlatter's case, and very slight disturbances in Storp's case (510 cm.) and in Ghedini's case (524 cm.). In Schlatter's case (192 cm.) the loss of fat was double the average amount. In Nigrisoli's case (520 cm.) the nitrogen and fat loss rapidly became nearly normal, and in Brenner's case (540 cm.) metabolism was normal except for slight disturbances of fat absorption two and a half months and one and a half years after operation.

There are therefore other factors apart from length of small intestine removed which influence metabolic disturbances. Among these factors may be mentioned the length of bowel remaining. This can be rarely known, but is really of greater importance than the length of bowel removed. The condition of the remaining bowel—*e.g.* if thin and atrophied, or if coils adherent, its power of compensation and of maintaining compensation must be seriously impaired; the pathological lesion present and the duration of the illness before operation must have a great effect on the recuperative powers generally, *e.g.* two cases died of recurrence of malignant tumours (Kukula, Storp), *e.g.*, three cases died of pulmonary tuberculosis (Maydl, Axhausen, Cannaday). Axhausen says: "The impaired intestinal absorption would not be without effect on the course of the tubercular process." These factors must always be remembered when comparing the results of experiments performed on healthy animals with the results of operations on the diseased or injured human subject.

The influence of diet on metabolic disturbances is significant and will be referred to later.

Urine.—Excess of indican or of the ethereal sulphates in the urine indicates an increase in intestinal putrefaction. An excess was commonly found in the urine of dogs subjected to extensive resections. In the cases under review, three reports on urine are given. There was no increase in Lexer's case (200 cm.), nor in my own case (228·5 cm.). An excess of ethereal sulphates in the urine was noted in Nigrisoli's case (520 cm.). In other respects the urine does not depart from normal in both animals and humans subjected to extensive resections.

Deductions from Experiments on Animals.—Experiments, chiefly on dogs, have been made by several investigators to fix the limit of safety in extensive resections of the small intestine, and to study the metabolic disturbances following such resections.

In 1892, Senn, after seven experiments, concluded that one-third was the limit of safety in intestinal resections, and that beyond that limit there was danger of diarrhœa, with increased appetite and death from marasmus. He noted a compensatory hypertrophy in the remaining gut in animals which had survived some considerable time.

In 1894, Trzebicki, after twenty-eight experiments, concluded that resection of one-half of the combined jejunum and ileum was well tolerated, but that resections of two-thirds interfered so much with digestive processes that life was impossible. There was incessant diarrhœa, undigested food in the fæces, sometimes vomiting, increased appetite but a fatal inanition. He found resections of the jejunum more serious than resections of the ileum. In autopsies he noted disappearance of the omental fat, dilatation but no hypertrophy of the intestine.

Trzebicki concluded that not more than 280 cm. (9 ft. 2½ in.) could be resected with safety—*i.e.*, half of the minimal length of the human intestine, which measures, according to him, 560 to 870 cm. (*i.e.*, 18 ft. 6 in. to 28 ft. 8 in.).

Monari, in 1896, stated that seven-eighths (87·5 per cent.) of the small intestine could be resected in dogs with no important interference with metabolism. Beyond this limit there ensued profuse diarrhœa, with loss of weight and fatal marasmus.

In autopsies he noted in dogs which survived for some time,

a compensatory hypertrophy and hyperplasia of the mucous membrane of the remaining gut with villi increased in number and in size. In dogs which died from inanition, he noted atrophy of the villi and desquamation of the epithelium. Monari believed one-half of the human intestine could be removed without serious metabolic disturbances.

Diliberti-Herbin, in 1904, found no difference in results from resecting the upper half of the small intestine in one dog and the lower half in another. Both dogs at first showed lack of assimilation of nitrogenous foods and fats but gradually improved, gained weight, and recovered perfectly.

Evans and Brenizer, in 1907, resected one-third to one-half of the combined jejunum and ileum in four animals which recovered. They noted a compensatory hypertrophy localised to the anastomosis. In two animals resections of 76 and 84 per cent. of the small intestine was followed by recovery, but in three animals resections of 86 to 92 per cent. resulted in death from inanition. In these three animals the limit had been exceeded beyond which compensation could be established, and no hypertrophy was noted at their autopsies.

Evans and Brenizer concluded that in animals one-third to one-half of the combined jejunum and ileum can be resected with safety, but that beyond this limit compensation may fail to be established, and death from inanition results.

Flint, in 1912, concluded from his experiments: "Dogs from which about 80 per cent. of the combined ileum and jejunum have been removed or short circuited may live indefinitely after the operation. The first effects of the operation give a profuse diarrhœa and loss of weight from both of which the animal slowly recovers. At the same time the resection of a smaller amount, *e.g.*, 65 per cent. of the entire intestine, may lead, notwithstanding a ravenous appetite and an unlimited diet, to changes which prevent the dog from recovering its well-nourished condition. In these animals the nutrition may be apparently normal, but they are nevertheless so sensitive to dietetic disturbances that a diet or conditions of any severity may introduce a fatal marasmus or enteritis."

Flint found that young, growing animals did not stand the operation as well as older dogs, but this influence of age is not apparent in the clinical records under examination. In Flint's own two cases, the resection of 204 cm. from a man, aged 29, resulted in death, preceded by violent metabolic dis-

turbances, while the resection of 100 cm. in an infant, aged 11 months, was followed by recovery, although at first there were severe digestive disturbances.

Flint also found that fractional resection was followed by quicker and easier recovery than where the entire resection was done at once.

Investigations into metabolism of these animals showed an excess of nitrogen and fat in the fæces as a direct result of the diminution of the absorbing surface of the gut. Profuse diarrhœa invariably occurred after the operation and the animals lost weight, being forced to consume the nitrogen and fat of their own tissues. Gradually, however, the excessive excretion of nitrogen and fats diminished through a restoration of the power of absorption from compensatory hypertrophy of the remaining gut. The animals gradually returned to normal nutrition although the fæces remained more offensive, due to intestinal putrefaction. The animals, however, remained susceptible to changes in diet, so that diets rich in fats or indigestible substances may again produce diarrhœa with excess of nitrogen and fat in the fæces.

The compensatory mechanism is only effective under favourable conditions, and in this respect is similar to compensatory hypertrophy in other organs, such as the heart, kidneys, etc. From the first carbo-hydrates are digested with greater ease than fats or nitrogenous foods. When compensation is established carbo-hydrates are completely utilised. From the studies in metabolism of these dogs with shortened intestines the appropriate diet appears to be one rich in carbo-hydrates and poor in fats.

Flint concludes: "The complete utilisation of the carbo-hydrates of the diet suggests the advisability of increasing these elements of the food, especially in some easily assimilated and usable form, like the simple sugars."

Functional Recovery dependent on Compensatory Hypertrophy of remaining Small Intestine.— Flint noticed a very distinct compensatory hypertrophy in the remaining gut in animals that had survived for a considerable time. There was no increase in length, but a marked increase in transverse dimensions, so that the gut looked twice the size it did at the operation. He concluded that the hypertrophy varied from 30 to 100 per cent., and involved the mucosa mainly. There was no increase in the number of villi, but 100 per cent.

increase in size, which equals 400 per cent. increase of surface. The crypts were enlarged in proportion to the enlargement of the villi. The epithelial cells of the hypertrophied villi were increased in size, and the goblet cells more numerous. No mitotic figures were seen. Compensatory hypertrophy may be adequate, and in these cases the animal makes a complete functional recovery and returns to a state of normal nutrition, although it may be susceptible to a breakdown in compensation under unfavourable conditions or diet. The compensatory hypertrophy may be partial, and in this case the animal recovers more or less for a time but later falls into a state of fatal inanition when compensation is strained. The compensatory hypertrophy may be absent, and in this case the animal suffers from profuse diarrhœa and loss of weight, and after consuming its own fat and nitrogenous elements dies from inanition. There is a limit beyond which a hypertrophic response cannot be obtained.

Flint's findings in animals are comparable to what is found clinically in human beings, although no compensatory hypertrophy has been reported in humans as yet. Brenner's case (540 cm.) is an example of a good recovery for a time from a sufficient but unstable compensation. A breakdown of the compensation, however, two and a half years after the operation caused a fatal marasmus. Post-mortem examination showed no compensatory hypertrophy, but atrophy of omentum.

Nigrisoli's case (520 cm.), showed at first great loss of fat and nitrogen in the fæces, but rapidly became normal with a gain in weight of 5·1 kilos in twenty-three days as compensation became established.

Miyaki's case (328 cm.), illustrates the more gradual recovery as compensation is established. At first there were three stools a day, but seven months later only one or two formed stools, with a gain of 9.5 kilos in weight.

Kocher's case (208 cm.), showed a slight instability of the compensation, as diarrhœa was apt to occur after carelessness in diet.

Werelius' case (365 cm.), is perhaps most illustrative of complete recovery following established compensation: At first continuous enteritis, which gradually subsided after careful dieting; thereafter partook of big beefsteaks without any disturbance, but tomatoes, corn and soups were evacuated quickly and undigested. Report three years after operation,

Synopsis of Cases additional to the 69 given in Cannaday's Table, "Annals of Surgery," 1919, lxix., 425.

No.	Operator and Reference.	Age and Sex.	Diagnosis.	Length Resected.	Method of Operation.	Result.	Investigation into Metabolism.	After-Condition.
70	Cannaday, J. E. *Annals of Surgery*, 1919, lxix., 425	30 M.	Ileo cæcal tuberculosis. Partial obstruction	300 cm., 10′ ileum. 20 cm., 8″ ascending colon	Lateral anastomosis, with transverse colon	Recovery	None	36 hours later, abdomen re-opened because vomiting persisted, and kink undone near anastomosis. 24 hours later, vomiting dark brown material, under local anæsthesia, catheter purse stringed into loop of small intestine. Vomiting then ceased. Catheter came away on 8th day and sinus closed 2 weeks later. Thereafter uneventful recovery. Left hospital at end of 4th week, wounds healed. At first 6 B. O. daily, later 3 B. O. daily. After discharge, caught cold after alcoholic excess, developed acute phthisis and died 2 months after first operation. P.M.—Remaining bowel measured: 5′ 7″ small intestine 4′ 9″ large intestine.
71	Littlefield, J. R. *Journ. Amer. Med. Assoc.*, 1919, lxiii., 835	22 F.	Gangrene of ileum following adhesions from operation on pus tubes 18 months previously	396½ cm., 13′ ileum at jejunum	End to side anastomosis	Recovery	None	There remained 6″ jejunum, 4′ ileum. Weight before operation . 110 lb. „ 1 month P. O. . 93 „ „ 3 months „ . 109 „ Eats well, but abdominal pain after coarse food and pastries. Resumed housework.
72	Wood, W. Q. *Edin. Med Journ.*, 1920, xxv., 61	62 F.	Strangulated umbilical hernia. Gangrene of ileum	218 cm., 7′ 2″ ileum	2 stage operation under local anæsthesia: (1) Resection. Paul's tubes inserted into ends of divided bowel. (2) Lateral anastomosis, with cæcum	Recovery	None	Fæcal fistula closed early. Patient well, able to be up and about. Died 2 years later from bronchitis.
73	Pirie Watson	63 F.	Thrombosis of mesenteric vessels	228.5 cm., 7½′ ileum	Lateral anastomosis	Recovery	Normal percentage of fat and nitrogen in fæces	3 years after operation. No digestive disturbances. Normal defecation, eats ordinary food, fully able for housework; states "never in better health." *Urine*—Very slight excess of indican, ethereal sulphates not increased.

partakes of anything just as before operation; has borne two healthy children and nursed the last herself; no special trouble during the pregnancies.

Influence of Diet on Metabolic Disturbances.—In the series of cases under review, 7 cases suffered from diarrhœa after certain foods. Among the special foods not well tolerated were milk polenta and fruit in one case, vegetables in another, meat in another, tomatoes and American corn in another, and soups in two cases. The resections varied from 192 cm. to 400 cm. in length.

In other cases where the resections were similar in length, it is definitely stated that ordinary diet was tolerated as well as before operation. It would therefore seem that certain articles of food are not well tolerated in special cases, and that where digestive disturbances are apt to occur, a diet such as is suggested by Flint should be adhered to, *i.e.*, carbo-hydrates, especially the simple sugars, in increased quantities; foods rich in nitrogen but poor in fats.

Conclusions.—(1) The term extensive is applied to resections of small intestine measuring from 200 cm. (6 ft. 7 in.) upwards.

(2) Such extensive resections may provide the only chance of preserving life, and it is instructive to know that numerous cases are recorded of operative recoveries with no digestive disturbances.

(3) The metabolic disturbances which follow extensive resections disappear if compensatory hypertrophy is established.

(4) Metabolic studies in animals suggest a diet rich in carbo-hydrates and nitrogen, but poor in fats.

References.—(In addition to those given by Flint, Moynihan and Cannaday.—[1] Flint, J. M., Bull. Johns Hopkins Hosp., 1912, vol. xxiii., p. 127. [2] Moyniham, Sir B., *Abdominal Operations*, 1918, vol. i., p. 455. [3] Cannaday, J. E., *Annals of Surgery*, 1919, vol. lxix., p. 425. [4] Littlefield, J. R., *Journ. Amer. Med. Assoc.*, 1919, vol. lxiii., p. 835. [5] Wood, W. Q., *Edin. Med. Journ.*, new series, vol. xxv., 61. [6] Blayney, A., *Brit. Med. Journ.*, 1901, vol. ii., p. 1456. [7] Kocher, *Operative Surgery*, 3rd Eng. Edit., p. 625, § 152.

Discussion.

Mr Struthers congratulated Mr Pirie Watson on the excellent result he had obtained, and said that one of the chief lessons to be learned from such a case was one of encouragement to persevere even in the presence of apparently desperate conditions so as to

give the patient a chance of recovery. He asked Mr Pirie Watson what the average length of time was between operation and the date of reporting in the successful cases.

Mr W. Quarry Wood said that it might perhaps interest the Society to hear the details of the case of resection of the small intestine which had come under his care. The case had been mentioned by Mr Pirie Watson. The patient was a woman of over 60 with a strangulated umbilical hernia. She had a hemiplegia a year before, the hernia had been strangulated for three days, and the pulse was 110, so that it was a very unfavourable case from the operative point of view. It was decided to employ local anæsthesia. On opening the sac numerous black coils of small intestine were exposed. The gangrenous portion was resected, and was found afterwards to measure 7 ft. 2 in.—4 in. less than in Mr Pirie Watson's case. A Paul's tube was fixed in each divided end and the intestine fixed to the abdominal wall, the rest of the wound being closed.

About ten days later the abdomen was opened in the middle line below the umbilicus—again under local anæsthesia. It was found that the portion resected was the lower ileum—the lower section being about a foot above the ileo-cæcal junction. The proximal portion of the intestine was united to the front of the ascending colon by a lateral anastomosis.

The patient made a good recovery. When she left hospital there was still a little discharge of intestinal contents from the original wound, but a letter from her doctor later stated that the wound healed completely, and that she was very well for about two years, and then died of bronchitis with failure of cardiac compensation. It was interesting to find that there were no disturbances of metabolism in this case.

PRIVATE BUSINESS.

Meeting—6th June 1923.

T. Douglas Inch, O.B.E., M.C., M.B., Ch.B., D.P.H., was admitted a Member of the Society.

EXHIBITION OF SPECIMEN.

Dr Watson-Wemyss showed a specimen of a chronic **gastric ulcer** of unusually large size.

DISCUSSION ON FOCAL INFECTION IN RELATION TO DISEASE.*

Opened by J. LORRAIN SMITH.

A comparison of the development of infection in a septic wound, in a case of diphtheria, and in a case of tuberculosis, defines the conditions in which infection is established by the formation of foci.

The most typical focal infection occurs in a case where bacteria conveyed by the circulation settle in definite sites in the tissues. The problem is to determine the factors which lead to the localisation of an infection which may become generalised.

The lymphatic system intercepts and destroys infection. When the infection becomes more severe the intercepting stations become foci in which the normal mechanism is disorganised and the bacteria grow and produce toxins. The lymphatic system may therefore be described as a focal mechanism.

The circulation of the blood partakes also to some extent of this focal character, and in certain organs, as for example the spleen and liver, there is a mechanism by which bacteria are arrested. Further, this arrest of emboli in blood capillaries, and especially in areas of terminal blood-vessels, brings about the formation of foci.

The question, however, still remains why the foci are formed in certain defined areas.

A consideration of the distribution of toxic effects introduces another localising process. The action of physiological and pharmacological substances is restricted and limited according to tissue function. Toxic effects are similarly restricted so that the tissues show a selective action. In many cases of severe toxic poisoning the effect is still more definitely localised in the form of focal necrosis.

The localising effect which is here exemplified differs in distribution from the localising of infection. The contrast between the two effects is seen in general tuberculosis, where the distribution of foci of infection does not occur in all the tissues which suffer from the toxins of the bacillus.

* Held 4th July 1923.

It is therefore suggested that the influence of toxic effect in determining the distribution of infection is more or less confined to the structures of lymph or blood circulation and to the disorganising of their special mechanism.

The liability of tissues which have been the seat of a local lesion to become foci in the course of a subsequent infection may be explained on this hypothesis.

The same conclusion may be drawn from recent investigations on the experimental production of focal lesions. Cole found in his investigation on the production of arthritis in rabbits by the injection of streptococci that in certain cases when the first injection failed to cause arthritis it was obtained when the injection was repeated. The toxic effect on the joint by the first injection localised the infection by the second injection.

These observations were repeated by Faber, who showed that a joint into which he had injected dead streptococci was sensitised, so that a subsequent injection of living streptococci into the blood produced arthritis. This effect he further found to be specific.

Rosenow has introduced another conception into the investigation of local infection. He claims to have demonstrated an elective power on the part of the bacteria. Bacteria which have been the cause of focal inflammation in a given tissue—the wall of the appendix, the gall bladder, the pulp of a tooth—have, according to Rosenow, acquired a faculty of growing in these tissues, and, if injected into an animal, will produce in that animal the same lesion as that from which they have been isolated.

These results, while still *sub judice*, have attracted much attention to the specific relation of bacteria to the tissues in which they form foci.

A comparison of various examples of infection shows that focus formation may, as in osteomyelitis, be found in the early stages of the disease; the infection progresses in the first place by the formation of foci and finally terminates in a general septicæmia. In typhoid fever, on the other hand, there is in the early stages of the disease a general infection of the blood (septicæmia); at the same time the formation of foci proceeds and may continue to a late period even after convalescence from the general infection.

It should also be noted that one disease may lead to the formation of focal lesions in a subsequent infection. A patient

who has suffered from rheumatism is specially liable to develop arthritis if subsequently infected by the gonococcus.

The sequence of events in these conditions may, it is suggested, be explained by damage to the normal protective focal mechanism.

Dr A. Logan Turner said: The title of this discussion, "Focal Infection in Relation to Disease," reminds me that, thirteen years ago, I introduced, at this Society, a discussion upon "The Part played by the Upper Air Passages as Avenues of General Infection." Although the two titles are closely allied, the subject, as wisely selected for this evening's discussion, covers a larger field, and thus should prevent too close concentration upon a limited area of the body.

Presumably, I have been asked to follow Professor Lorrain Smith because of the importance of the upper air passages in furnishing foci of infection in disease. It is not my intention to traverse the whole of the ground included in the area of the special department, but I will confine my remarks to one or two points. If one speaker endeavours to overtake too much, he interferes with the development of the discussion by others.

In recent years, the assistance of the Throat Department has been more frequently sought in connection with the possible existence of primary foci, and the number of diseases for which such help is desired continues to multiply, so that one is forced to consider whether there is not a tendency to overrate the possible relationship between a local focus and a general condition.

The Department is probably most frequently approached in connection with the rôle of the tonsil in relation to the so-called rheumatic affections, and it is on this subject that I wish to say a few words. While, in some instances, a focus of infection is easily recognised in the tonsil, in other cases, a decision on this point is by no means readily arrived at. Whether recognised or not recognised, I think it is wise, before condemning the tonsil, to make certain that all other possible foci of infection have been eliminated, such as, the nasal, post-nasal, and accessory nasal cavities, the teeth, the alimentary canal, and the genito-urinary tract. And even if all these sources be eliminated, then, to express a somewhat guarded opinion as to the effect, upon the disease, of removing the tonsils.

There would appear to be, at the present time, a tendency to overrate the malign influence of the tonsils, both in connection with rheumatic and with other affections (I am not concerned with tubercle), and thus by their injudicious removal in the wrong class of case, to cast a slur upon an operation which, when employed in suitable cases, gives eminently satisfactory results.

The position may be expressed in the two following questions:

How often does the faucial tonsil play the part of a primary focus in rheumatic affections? and, How are we to estimate, in any given case, that the tonsils contain the focus?

In a recent paper upon "The Prevention of Heart Disease," F. J. Poynton states that he is a believer in local foci of infection, and that the most important local focus in rheumatic heart disease is probably the tonsil. "At the same time," he continues, "many will agree that the removal of tonsils does not prevent further attacks; nevertheless, the removal of *unhealthy* tonsils in rheumatic children is recommended, but that their wholesale removal in such children is not to be recommended, unless there is evidence that they are diseased." In this statement we find expression of the very difficulties which are set forth in the two questions just asked. Let us look at some of the published results following the removal of the tonsils in rheumatic affections.

Crow and Watkins, of the Johns Hopkins Hospital, have published a series of after-histories of such patients undergoing tonsillectomy: they found a recurrence of arthritic symptoms, repeated attacks of rheumatic fever, and a recurrence of chorea after a mild coryza or pharyngitis.

Hunt and Osman, working at Guy's Hospital, are about to show that of 144 patients admitted with acute rheumatism, there was a recurrence of the infection quite as frequently amongst those who had had their tonsils removed as amongst those who had not.

Our own more recent observations in hospital have been published in the Reports of the Ear and Throat Department for 1921, by Dr Whitton, Clinical Assistant. Of 23 cases of rheumatism which underwent tonsillectomy, 14 were cured, 3 improved, while 6 were not affected by the operation. Of 11 cases of chorea, 3 were cured, 4 improved, and 4 not affected. Combining the two groups, making 34 cases in all, 17, or 50 per cent., were cured.

It is obvious from these various published reports that many cases are operated upon, and that tonsils bearing no relation to the disease, or possibly only in part responsible, have been regarded as the cause.

Until we are able to form some better estimate of the part played by the tonsil as a focus of infection, unnecessary operations upon that structure will continue to be performed.

I suggest, therefore, that in order to advance the subject, a much closer co-operation is necessary between the laryngologist, the bacteriologist, the general practitioner, and the bio-chemist. There should be less of the water-tight compartment system, in which so much of our work is done. From the bacteriologist we wish to learn more of the pathogenicity of the organisms inhabiting the tonsil crypts,

and whether, because certain organisms are present, then the tonsil must be regarded as diseased; laboratory experiments should be linked up with clinical experience: from the general practitioner, a careful previous history of the patient and a still more careful "follow up" record of the cases operated upon: from the bio-chemist, a report upon the metabolism in cases of chronic arthritis, both before and after operation, as foci of infection may be only one element in the causation of these cases.

By grouping the observations from all these sources, we, as clinicians, whether laryngologists or practitioners, would be in a better position to determine upon the part played by the tonsil in this disease and to advise upon the question of its removal, and thus to avoid unnecessary operations.

Looking back, in a general way, upon one's experience, I would say that, of the cases of this class upon which I have operated, more had been followed by disappointing results than by cure of the general infection. Possibly some of these operations had been performed too late, and the generalised infection had perpetuated itself even after removal of the original focus.

Professor Russell said that he had listened with great pleasure to the charming introduction by Professor Lorrain Smith of the subject before the Society for discussion. He was so much impressed by it that he had difficulty in making any comments on it. The subject was very large and covered a varied field, and he was not prepared to go into detail. The question of the preparation of the field for infection by an organism by absorption of the toxin produced was of great significance but was not at present determined. With regard to the whole question of susceptibility and insusceptibility it always seemed to him that it depended primarily on the chemico-vital constitution or composition of the individual. Individual variations on this side were infinite. He knew a medical man in years past who, whenever he had to attend a patient with typhoid fever, had a mild attack himself; other instances of a like susceptibility to other infective fevers were met with, and to his mind the only explanation was a chemico-vital variation on the part of the susceptible individual. He did not propose to elaborate this aspect of the subject and left other aspects of it to be dealt with by subsequent speakers.

Dr Chalmers Watson emphasised the importance of a thorough examination of every source of sepsis including nasal, dental, genito-urinary, and intestinal. He referred to the frequency and probable importance of bacteriuria in many cases where, through lack of investigation, its presence was not determined. In connection with the possibility of intestinal auto-intoxication and infection, a difficulty

arose in regard to the great limitations in our knowledge of the intestinal flora and the part played by it both in health and disease. He shared the view of a previous speaker as to the frequency and importance of fibrositis arising from focal infection from one or other of the mucus surfaces. The routine post-mortem examination made on many medical cases gave, unfortunately, little information of value to the clinician. A condition of dilatation—local or general—of the bowel, and of catarrh, often of a local kind, were extremely common and were too commonly classified by the pathologist as "Post-mortem Findings." This view had the merit of obviating the need for the further investigation which was, from the clinician's point of view, essential if any real progress was to be made in the study of focal infection from the intestinal tract.

Mr Wade said that in his opinion the subject of Focal Infection was particularly suitable for discussion in the Medico-Chirurgical Society as it could be approached from the standpoint of the bacteriologist, the specialist, and the general practitioner. He was particularly anxious to hear from the bacteriologists whether they were in agreement with the remarkable results obtained by Rosenow, whose work, if substantiated, appeared to him to be the most valuable contribution to the science of bacteriology that had been made in the last twenty years. Prior to Rosenow's investigations it had been generally accepted that the factor that determined the circulating virus to the region in which it gave rise to its secondary manifestations was the presence there of an area of lowered resistance to infection in the tissues, which was usually the result of some previous traumatism, as where an acute infective osteomyelitis developed in the tibia of a young boy, the bone having been previously damaged by some slight injury. According to Rosenow's work the selective affinity of the germ for the region in which it ultimately settled was due to another cause. He claims to have proved that "it is in the focus of infection that changes in virulence occur, and the different affinities for various structures are acquired. The focus of infection is not only the place of entrance but also the place where organisms acquire peculiar properties to infect other areas throughout the body."

The place of localisation of the germs after they have gained entrance into the blood-stream is due neither to accident nor there being situated there an area of lowered local resistance, but is attributable to certain delicately balanced conditions which must prevail before localisation and growth of bacteria can occur in a given tissue. His idea is that localisation may be determined by peculiar properties in different strains of the same species of bacteria, or with even the same strain when subjected to different conditions.

As a Resident under the late Sir Thomas Fraser, Mr Wade had

been taught to realise the importance of focal infection as a cause of many so-called rheumatic ailments. He also thought that in this Society and in this city the pioneer work of William Hunter should not be forgotten, who claimed many years ago to have demonstrated the etiological relationship between oral sepsis and pernicious anæmia, and in doing so laid the foundation of a branch of research that had yielded many valuable results.

Mr John H. Gibbs said that he was frequently confronted with the difficulty of trying to determine the part that oral sepsis played in the illness of a patient. Oral sepsis as an ætiological factor was perhaps overrated, whilst on the other hand its malign influence in retarding the recovery of patients from almost any disease was underestimated. The principle on which he gave advice was that the mouth must be clean, and that even if it were unlikely that the state of the mouth was the cause of the illness, the teeth must be removed if for any reason the mouth could not be kept healthy without doing so. He was quite certain that the stay of patients in hospital could be materially shortened by putting their mouths into a healthy condition at the very outset of their treatment.

Dr Cranston Low said that the Skin Department was responsible for sending to Dr Logan Turner a good many cases in which focal infection of the nose or throat was suspected of being the cause of an eruption. Of these cases, lupus erythematosus was probably the commonest. There is a great deal of evidence that these cases are due to focal infection with the *Streptococcus longus* either on the tonsils, adenoids, gums, or bowel. Some two years ago the late Prof. F. D. Boyd had a case in his ward suffering from an acute bronchitis with *Streptococcus longus* in the sputum. The patient had had a typical lupus erythematosus on the face for many months. After recovery from the bronchitis, as she had a very septic mouth with marked pyorrhœa of both jaws, all the teeth were extracted, and within ten days the lupus erythematosus had disappeared. She remained well for six months, and was readmitted with another attack of acute bronchitis again with the sputum teeming with the *Streptococcus longus*. Within a few days the lupus erythematosus reappeared on the face. Dr Barber of London has reported numerous such cases due to infection of the gums, tonsils, or bowel, in which treatment by removal of the foci or inoculation with autogenous vaccines caused a rapid disappearance of the lupus erythematosus. The other class of case in which focal infections may provoke a skin rash is in urticaria. Urticaria is undoubtedly a sensitisation phenomenon exactly similar to the rash in serum sickness. Some cases were due to sensitisation to foods, but others, especially in adults, were due to a bacterial

sensitisation. A case recently under the speaker's care was a lady of sixty years of age, who showed an ordinary recurring urticaria all over the body. Cutaneous food tests were found to be negative, and dieting had no effect. About two months after being seen, the patient developed pain in the jaw and went to her dentist who extracted two teeth. Within twenty-four hours the urticaria ceased and has not recurred. The other diseases which have been suspected of being due to focal infection are prurigo, chronic forms of so-called eczema in adults and alopecia areata, but in these the association of focal infection with the disease is not so well proved as in urticaria and lupus erythematosus.

Dr Low also expressed some disappointment that Prof. Lorrain Smith had not laid more stress on the part played by sensitisation in infection. The two conditions could not be separated. The question always arose in infections, as to how many of the changes were due to the toxins of the invading organism and how many to sensitisation to the bacterial proteins. In true anaphylaxis and other forms of sensitisation the evidence went to show that the fixed cells played as great a part as the blood. If the fixed cells of any tissue became sensitised to the invading organism, then, wherever that type of tissue-cell existed, if the organism was circulating, it would react with that cell. That might explain why, in certain infections, only one type of tissue is affected in each case. One kind of organism might produce different diseases according to which tissue-cell was sensitised. In dermatitis venenata due to the primula the skin-cell alone is sensitised, and if the leaf of the primula plant were rubbed on the skin a dermatitis venenata always resulted, whereas the leaf might be applied to the mucous membranes of the mouth or swallowed with impunity. So in cases of rheumatism, if the cells of the synovial membrane were sensitised, arthritis resulted; if sensitisation of the fasciæ occurred one got lumbago; if the large nerves, sciatica, and so on.

With regard to the removal of foci the case was often seen too late to do much good by the removal of the primary focus. It did not do much good to remove the tonsils if small infected glands were left or the bowel lower down had become infected. The speaker did not approve of the wholesale removal of teeth on the chance of curing a patient. He thought that that should not be done unless the probability was that that was the only focus of infection.

Professor Meakins said: There are several points to which I would like to draw attention. In the first instance, I am sure it has been the experience of many to observe very pronounced hereditary tendency to infection. There have been published, and I have been able to compile, a number of very complete examples of this tendency to specific infection passing through three or four generations. Not only

is there a tendency to infection in the individual, but also there would appear to be a definite predisposition of certain tissues or organs, in members of families, to become the site of or to show signs of premature degeneration. The older physicians when they spoke of rheumatic, cardiac, renal, and other diatheses had a good deal to substantiate their diagnosis. The time came, however, when the enthusiasm for the specificity of infection seemed to rule this idea out of court. I think now, however, there is very good reason to pursue the subject in the light of both the specific organism and the specific predisposition or susceptibility.

In regard to focal infections as such, it seems to me a very important question to decide, where an infection has become general and there have been metastatic areas of inflammation, whether the latter may not be of even greater importance than the original portal of entry. I do not mean to infer that the original site of infection should not be removed, but even though this be done the metastatic areas of infection may, and often do, continue to be the origin of further metastases. Sir Harold Stiles has made reference to the occurrence of fibrositis, and I would like to draw attention to how this lesion and also many others are associated with definite metabolic disturbances; it is not at all clear at the present time which may be the cause and which the effect. It is well known that individuals may be susceptible to the products or the chemical constituents of bacteria as they are susceptible to definite chemical substances. This in the past we have described as idiosyncrasy. The present evidence would indicate that the organism, either locally or in general, may be susceptible to certain chemicals. Such chemicals may be derived from bacteria, food, etc. They may obtain entrance through the mucous membranes, may be ingested, or be inhaled. Such substances are not necessarily poisonous to the average individual, and often their toxicity is determined by the specific susceptibility of a particular tissue or of the organism as a whole.

Dr Goodall referred to the extraordinary susceptibility of joints to infections. Besides the numerous primary arthritic conditions the joints might be involved in such diverse infections as scarlet fever, typhoid, dysentery, and malaria. He spoke of experimental research work which he thought touched upon one of the many fringes of the subject. He had injected hæmolytic agents into animals and found that small doses caused secondary anæmia while massive doses produced something which resembled pernicious anæmia. By no intermediate dose could an intermediate blood picture be obtained. This seemed to suggest that differences in the dose of a noxious agent might not only alter the severity but the nature of the reaction. In some of these experiments there was an extraordinary change in the

appearance of the endothelial cells of the splenic sinuses. It came to resemble columnar epithelium, and it might be suggested that a small dose might so alter the character of phagocytic cells that they reacted differently to further or larger doses—a kind of histological sensitisation. In connection with anæmia it was remarkable that a case of secondary anæmia becoming pernicious had never been reported. He had no doubt that pernicious anæmia was a focal infection of the bone marrow.

Professor Robertson said he wished in the first place to refer to certain clinical observations of his, which seemed to support the particular views of Rosenow to which several speakers had referred. Physicians in charge of mental hospitals had very peculiar opportunities of studying outbreaks or small epidemics of influenza among the population under their charge. They saw far more cases than the general practitioner because every case, however slight, was observed and brought to their notice. He had been struck by the fact that in many of these epidemics, which he himself had observed, particular symptoms often predominated—for example, in one small epidemic there were no less than ten cases of suppuration from the ear. In other epidemics there had been cases of jaundice. It seemed to him therefore that these clinical facts seemed to support Rosenow's views that micro-organisms might acquire special qualities which enabled them to seek out particular tissues within the body.

He would first state how surprised he was that it was not universally admitted that the brain and nervous system were the organs and tissues of the body most highly sensitive to the effects of the toxins of micro-organisms. It was true that focal infection did not occur in the nervous system with very great frequency but it was predisposed to the actions of toxins—such as that of diphtheria, to which Prof. Lorrain Smith had referred. There seemed to be stronger clinical affinity between the nervous tissues and organismal toxins than between the latter and any other tissues in the body. It was true that destruction or death of tissue did not always occur, but the metabolism of the cell was so affected that its function was deranged, and in the case of the brain this became visible by the production of mental symptoms.

There were two other features connected with infection which were important in his special subject, to which reference had not been made, and these were virulence and chronicity.

If the toxins were virulent then the disorder of mental function was so great that they had a form of insanity known as delirious or confusional insanity. This was characterised by a confusion of the intellect, by multiple hallucinations and by loss of memory of the events of the illness after recovery. The symptoms produced by this condition were so definite that it was possible whenever they were observed to state that the patient was suffering from a toxæmia of

some kind or another. He recalled a case of his in which he diagnosed "toxæmia." The blood was examined and in a smear a bacillus was found. A culture was then made of the blood and a pure growth of the organism of enteric fever was found. In this case, therefore, as a result of these special mental symptoms, the particular infection from which the patient was suffering was diagnosed, although the general practitioner and the consultant, who had been called in, had failed to diagnose the condition.

There is, however, another class of case involved. Infection in which the toxin is mild and non-virulent, but its action is prolonged, perhaps lasting for many years. In these cases there is the daily absorption of a certain amount of toxin, and although no very obvious symptoms are produced, nevertheless by the lapse of time such changes are ultimately produced in the nerves that insanity develops, and very often this insanity is of a chronic and incurable nature.

The infection in these cases is so mild that the attention is not directed to it by such signs as rise of temperature or a leucocytosis. The focus may be in any part of the body, but it is believed that if this be in the head or throat, there is a greater tendency to mental disturbance owing to the fact that the toxin may travel along the lymphatics of the nerves and thus obtain a very easy entrance to the cranial cavity.

The effects produced by alcohol enable one to see readily the difference between these two forms of infection and the resulting disturbance.

In the first place, there is the man who drinks greatly to excess—perhaps one or even two bottles of whisky a day, corresponding to the virulent toxæmia. Such a patient passes into an acute delirious condition, which is strictly analogous to that already described.

On the other hand, you have the case of the man who drinks only small quantities of alcohol, but who is constantly indulging in it. No one can say that he has ever seen this man under the influence of alcohol, he has never been drunk. But, as a result of this constant nipping like the result of the constant absorption of small doses of non-virulent toxins, the patient after some years suffers from such degenerative changes in his brain that the alteration and deterioration in his mental condition is recognised by all.

Owing to the fact that permanent changes have possibly taken place in these cases, he is very much in sympathy with the work of Sir James Mackenzie at the Clinic of St Andrews, as early treatment offers the greatest hope. On this account, in all subjects with nervous inheritance anything of an infective nature is dangerous and should be treated. Example is better than precept, and he may conclude by saying that a short time ago, as a result of a tooth being infected in

a dental operation there developed an abscess at the root. His temperature the first night was 104°, but the trouble soon subsided. After a year he found that the abscess still persisted. In one of the medical papers he then read the remark by a medical man that he would as soon keep a leopard in his house as tolerate the existence of such an abscess. He at once went to Mr Guy and had his tooth extracted.

Dr John Thomson, in connection with what had been said about families in which various infections showed a tendency to affect certain organs and tissues specially, referred to his experience of family peculiarities in the distribution of congenital syphilitic lesions. In one family of three, all the children died with intercellular cirrhosis of the liver and general debility. The infants had shown almost no rash and scarcely any snuffles. In another, the first three out of four children suffered severely from epiphysitis. In a third the only two children who, after early symptoms of syphilis, had survived to later childhood, had multiple periosteal nodes on the long bones. In a fourth family, four children out of seven showed extensive choroiditis.

Dr Frederick Porter said that he was surprised the discussion had not produced an endocrinologist.

He illustrated the following cases:—

1. A woman suffering from myxodœma and pyuria in whom the pyuria disappeared after a course of thyroid.
2. A boy with marasmus and pyuria in whom the pyuria disappeared by treatment with thyroid.
3. A woman with an obstinate pyuria who had received a prolonged course of vaccine therapy and urinary antiseptics with no benefit, but was cured by a course of suprarenal extract and parathyroid. Those cases led him to believe that more knowledge of the subtle processes of metabolism would lessen the obscurity of disease and possibly make the work of the bacteriologist in future unnecessary.

He stated that we had still to discover the explanation of susceptibility and resistance to disease.

THE NUTRITIONAL TREATMENT OF TUBERCULOSIS.*

By Professor CLEMENS PIRQUET, Vienna.

For the purpose of teaching we regard tuberculosis in a similar way to syphilis, in so far that we make the difference between the primary, secondary, and tertiary stages.

The primary stage includes the primary lesion of the corresponding lymphatic glands, and this, in the vast majority of infections on the Continent, means a primary focus in the lungs and an infection of the bronchial glands.

The secondary stage comprises the transportation of bacilli and formation of tubercles in all parts of the body—bones, joints, subcutaneous tissue, the skin, brain, and so on.

By the tertiary stage we mean the tuberculosis of the lungs —phthisis. This stage occurs rarely in children, and the disposition of the lungs for cavity formation seems to have some connection with sexual development as it begins during puberty —in girls some years earlier than in boys.

The prognosis of tuberculosis depends partly on the situation and the extent of the foci, partly on the age of the patient, and partly on his state of nutrition.

As to age, new-born children have almost no resistance against tuberculosis. If a child is infected soon after birth, the disease is practically fatal: whereas even in the second half of the first year the resistance allows many patients to survive. From the sixth to the fourteenth year the infection of tuberculosis seems to be practically innocuous, as it leads mainly to primary symptoms not followed by any secondary development. During, and soon after, puberty the prognosis is less favourable on account of the dangers of a tertiary stage in this period.

As to the state of nutrition, this has a great influence on the spreading of the disease inside the body. The antibody formation against tuberculosis seems to have a near correlation with metabolism, in as much as only a certain surplus of nutrition allows a good antibody formation. On the other hand, if the organism lacks food, the bacilli seem to be able to get through the walls of tissue and make new colonies in the body. Periods of lack of food or of lack of appetite play a big

* Read at a conjoint Meeting of the Medico-Chirurgical Society of Edinburgh and the Tuberculosis Society of Scotland, 20th July 1923.

rôle in the history of advanced cases. As to the therapeutic value of nutrition, I think that the main therapeutic agent in the different climatic resorts celebrated for the cure of tuberculosis is the appetite, acquired by patients in new surroundings, where they live in the open air and get good food and are free from their home worries. Now, we need not depend upon spontaneous appetite and do not require to stimulate the appetite only by the suggestion of a new *milieu*. If we prescribe the right quantity of food and make the patient eat that quantity, we are independent and freed from the uncertainties as to whether the health resort will act on the patient or not.

The *prescription of food* is made after the so-called "Nem" system. This consists of two new things. The one is a new unit of nutrition instead of the calory. I use a unit which is easily understood by a mother or a cook—that is milk.

One gramme of average milk is called nutrition element milk—abbreviation "nem." The multiples are called after the metric system—1 hectonem = 100 units, or the food value of 100 grammes of milk, or approximately, 1 quart of milk. All the different food stuffs are compared to milk in their combustible value—for instance, 1 gramme of flour = 5 grammes of milk. Therefore we say 1 gramme of flour contains 5 nems. The practical unit for composing meals is the hectonem. We, so to speak, build them up by different single bricks, each of which has the value of 1 hectonem. If, for instance, we had to give a breakfast of 8 hectonems, we could best do it in the following way :—

	Grammes.				Grammes.	
1.	100	Milk	with water and tea.	5.	8·5	Butter.
2.	100	Milk		6.	30	Bread.
3.	17	Sugar		7.	20	Ham.
4.	30	Bread.		8.	30	Jam.

The working of the kitchen has to be based on these principles and the food value of all the food stuffs carefully calculated.

The second principle in the "Nem system" is the *individual determination of the food requirements*. This is based on the square of the sitting height of the individual. The sitting height is the distance from the surface of the seat on which the body rests to the top of the head. This is ascertained by simply measuring the distance between the

horizontal seat and a horizontal board resting on the head. The sitting height is the most important measurement of the human body as it has close relations to weight: the cube of the sitting height in centimetres in a normal adult is about equal to the weight in decigrammes, or to ten times the weight in grammes. A man of the sitting height of 90 centimetres has an approximate weight of 90 × 90 × 90, that is, 729,000 decigrammes or 72·9 kilogrammes. The sitting height has also a relation to the intestinal tract—the length of the small intestine and colon being about ten times the sitting height of the individual.

Nutritive requirements do not go parallel with the body-weight, but with a second power corresponding not to a cube but to a surface. This surface was got by previous authors by measuring the outside skin or taking the square of a third root of the weight. I get at such a surface in a much simpler way by squaring the sitting height (as this relates to a third root of the weight), and in order to give a vivid conception of this surface to the layman, I compare it with the intestinal surface. As I said before, the length of the bowels is about ten times the sitting height, and I may add that the width of the intestinal canal averages approximately one-tenth of the sitting height. The surface of the bowels, therefore, would be ten times the sitting height by one-tenth of the sitting height = the sitting height square. I may repeat again, I do not consider the intestinal surface an exact conception. It is only a comparison which is easy to imagine.

In a long series of experiments I watched the spontaneous intake of food. Children and adults were allowed to take as many "hectonem bricks" as they wanted, and we compared afterwards this amount with the square of their individual sitting height. Very simple rules could be deducted from this experiment.

The *maximum* of intake corresponds about to 1 gramme of milk per centimetre square of the supposed intestinal surface, or 10 decinem per square centimetre of the sitting height square (siqua)—expressed shortly, 10 dnsq. If one gives more food than this amount there is a danger of putting the intestinal machine out of order.

The *minimum* is the amount necessary for the maintenance of body-weight in a person who lies in bed quietly—therefore

the amount necessary for internal work, movements of the heart and lungs, secretions of the big glands, etc.—and is about 3 decinemsiqua (3 dnsq.).

The third conception is the *æquum*—the amount necessary to keep the same body-weight alongside with a given amount of exercise—to keep, for instance, a working man at the same weight in spite of manual labour. This amount depends a great deal on individual activity. We reckon 1 decinem in excess of the minimum for people with a chiefly sedentary occupation, like a clerk; and 2 decinem are added to the minimum or 5 decinemsiqua are prescribed in all for a man with a partly-walking occupation, like a doctor.

The last conception is the *optimum*, the amount which a physician would prescribe in a given case where he wishes to allow for changes in body-weight. For instance, we always add 1 decinemsiqua to the *æquum* for children, as we want them all to grow; we add 2 decinems for children who are meagre, as we want to fill them out. On the other hand, there may be adults where the *optimum* is lower than the *æquum*, because we want them to lose flesh.

Most of the tuberculous children, whom we have under observation (100 on the roof-garden of my hospital and 80 in a convalescent home) are given 7 decinemsiqua: 3 for internal rest, 7 for exercise and growth, and 1 for fattening.

If we want a child to eat a certain quantity of food for a day we have to divide this amount properly into the single meals. If we have a child of, say, 60 centimetres sitting height who ought to get 7 decinemsiqua, the total daily amount therefore would be $60 \times 60 \times \frac{7}{10}$ nems, or $360 \times 7 = 2520$ nems = roughly, 25 hectonems. These 25 "bricks" have to be divided into five meals, at intervals of three hours. If we have breakfast at 7, we would have the second breakfast at 10, luncheon at 1, tea at 4, supper at 7. We generally give 3 hectonems at second breakfast and 2 at tea and divide the remaining hectonems into the three main meals—for instance here—25 less $5 = 20$, $20 : 3 = 6\frac{2}{3}$—we give 6 hectonems at breakfast and 7 at dinner and supper.:—

Time of meal	7	10	1	4	7
Hectonems	6	3	7	2	7

As we have to feed a great many children of different sitting heights, we put all those children together who get a

similar prescription and "nutrition classes" are formed, getting respectively, 20, 25, 30, 35 and 40—and so on—hectonems. The children are seated at different tables according to their class. The hectonems are distributed by means of a balance for the solid food and by graduated dippers for the fluids. The children have to eat all that they get, not only every kind of food but all the amount prescribed. As all the children at the table have the same amount, this is very easily supervised. A side-issue of this way of feeding children is the absence of remnants. Everything has to be eaten. This means a great saving in comparison with the usual method in a children's hospital.

I want to say a word about the application of these food principles. Very largely owing to the American Child Food work in Austria—Hoover's Organisation—we were enabled to feed 400,000 Austrian children in this scientific way. They got one meal a day containing from 5 to 15 hectonems, and we had the great advantage of making a scientific investigation of the state of the nutrition before, during, and after the period of food distribution. I may say here that I think that this American work has been the greatest battle ever fought systematically against tuberculosis, as most of the children had an infection, and we prevented it from spreading in not allowing them to fall into a bad state of nutrition.

This whole line of feeding work is a very satisfactory one, but it depends not on the doctor alone but also on the cook, and you cannot come to any accurate results unless the kitchen is directed by a superintendent who absolutely follows the doctor's orders.

I hope that many of you will give this new system a fair trial, and that it will prove satisfactory to you.

I thank especially Sir Robert Philip for his kind invitation. His institutions are a model for the whole world, and his system of dispensary work co-operating with the different kinds of tuberculosis hospitals is an ideal one for a systematic fight against tuberculosis. I am hoping he will add the nutritional treatment to his different methods, and especially to his method of detuberculisation.

Professor Meakins, on behalf of the Medico-Chirurgical Society, and Sir Leslie Mackenzie, on behalf of the Tuberculosis Society, proposed a vote of thanks which the President conveyed to Professor Pirquet.

INDEX

Index

Index

Index

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